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INTRATHORACIC GOITRE: ITS PREVALENCE IN SYDNEY METROPOLITAN MASS RADIOGRAPHY SURVEYS.

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In published papers on intrathoracic goitre, much space is devoted to modes of classification and to problems of nomenclature; but a simple and adequate definition of intrathoracic goitre is the demonstrable presence of goitrous tissue below the plane of the thoracic inlet. Such tissue may be demonstrated radiologically, by scanning with a directional probe after a tracer dose of radioactive iodine (I^{131}), or most decisively at operation. The plane of the thoracic inlet joins the upper margin of the body of the first dorsal vertebra, the neck and inner borders of the first ribs, and the jugular notch of the sternum.

For the purpose of this paper, a given subject has been accepted as having an intrathoracic goitre when this diagnosis has been made radiologically in the chest clinic of the Anti-Tuberculosis Association, and when subsequent reexamination of small and large chest films by us has failed to throw doubt on the diagnosis.

Material and Results.

For information on the scope and technique of these mass radiography surveys, reference may be made to earlier papers by one of us (Rubinstein, 1955, 1956). Miniature chest films (70 millimetres) of good quality are obtained and are read by a skilled radiologist and a chest physician working independently. When an abnormal shadow is found, the person concerned is called back to the clinic and a large chest film is taken. This and clinical inquiry resolve doubt as to diagnosis in a high proportion of cases. Radiologically, the intrathoracic shadow can often be seen continuous with a soft-tissue shadow in the neck, and when the patients were called back for their large film the presence or absence of a cervical goitre or the evidence of previous thyroidectomy was noted (positive data, of course, greatly increase the probability that the mediastinal shadow is goitrous).

Up to December 31, 1956, 234 subjects had been diagnosed as having intrathoracic goitre by mass radiography survey. In 11 cases of this number the X-ray films were missing and the patients could not be called back to the clinic; they have been excluded from our study. Also in the final scrutiny of films from the remaining 223, and from consideration of the available clinical data, 29 were excluded

[1] Retail Traders' Association Research Fellow.

[2] Work done in the Joan Bonamy Surgical Research Laboratory and aided by a generous grant from an anonymous donor.

TABLE I.

Number of Persons Mass Radiologically Examined in Sydney Metropolitan Area, and Number of Subjects with Intrathoracic Goitre in Sex and Age Groups.

Age Group. (Years.)	Males.		Females.		Total.	
	Number of Patients.	Number Radiologically Examined. (Estimated.)[1]	Number of Patients.	Number Radiologically Examined. (Estimated.)[1]	Number of Patients.	Number Radiologically Examined. (Estimated.)[1]
Under 14	0	1389	0	1444	0	2833
14 to 19	0	39,486	0	50,724	0	90,210
20 to 24	0	55,002	1	52,047	1	107,049
25 to 29	1	66,557	1	49,481	2	116,038
30 to 34	0	60,180	1	45,022	1	105,202
35 to 39	2	52,420	1	42,113	3	94,533
40 to 44	2	49,722	3	41,675	5	91,397
45 to 49	3	44,524	8	38,590	11	83,114
50 to 54	4	38,822	12	36,164	16	74,986
55 to 59	4	30,920	24	30,946	28	61,866
60 to 64	7	28,339	33	28,399	40	56,738
65 and over	22	40,608	60	42,078	82	82,686
Not stated	1	684	4	423	5	1107
Total ..	46	508,653	148	459,106	194	967,759

[1] These estimates for sex and age distribution of the total population examined (967,759) were derived from the known sex and age distributions in a large sample (192,297; Rubinstein, 1955).

because of doubt as to the diagnosis. This left a total of 194 accepted cases of intrathoracic goitre. Final proof of the nature of a superior mediastinal shadow may depend on surgical exploration and biopsy, and few of the present series of patients have been operated on. Thus some doubt may remain as to the nature of the opacity, especially when a cervical goitre is lacking. Actually 114 of the 194 patients were known to have a cervical goitre or history of thyroidectomy, and the total may have been higher, since of a group of 52 specially studied in the Unit of Clinical Investigation, 41 had a palpable cervical goitre or a history of thyroidectomy. The remaining 142 patients were examined in the chest clinic, where less detailed thyroid studies were made.

Altogether, we believe that our total of accepted cases may understate the true number, because in at least some of the 11 in which the films were unchecked the diagnosis was probably correct. Also, it is inherently probable that in surveys aimed primarily at detecting tuberculosis, some intrathoracic goitres will not have been reported. It is relevant that the detection of small superior mediastinal masses is difficult because of the conglomeration in this area of great blood vessels, as well as the trachea and œsophagus, though deviation of the trachea is itself a tell-tale sign. Moreover, soft-tissue detail is here obscured by the overlying *manubrium sterni*, clavicles and flattened first ribs.

The first full-scale mass radiography survey began in Sydney on April 30, 1953, and 891,560 films were taken up to December 3, 1954. The metropolitan area of Sydney is divided into municipalities, and each in turn was declared by the Government a "proclaimed area", it being compulsory for all residents aged over fourteen years to undergo radiological examination of the chest. It is estimated that the first survey included 88% of the eligible population. Inquiry at the time elicited the fact that approximately 50% of the people were having their chests radiologically examined for the first time. The second survey commenced two years later, and up to December 31, 1956, approximately 508,000 persons were examined radiologically. In the second survey only about 15% of persons said that they had not been radiologically examined previously. It may thus be estimated that some 967,759 persons have been radiologically examined in the metropolitan area of Sydney in the course of these two surveys (891,560, *plus* 15% of 508,000), and it is from this pool of material that the 194 accepted cases of intrathoracic goitre have been drawn. The survey has covered all varieties of suburb, business, industrial, and residential.

Table I shows the number of subjects with intrathoracic goitre detected in the different age groups of the two sexes. The frequency with which females are affected is more than three times that of males. In both male and females the later age groups provided most of the cases —63% of those affected were aged sixty years or older.

To arrive at the prevalence of intrathoracic goitre per 100,000 of the population radiologically examined (Figure I), use has been made of the known sex and age distributions of a very large sample, 192,297 in number. The sex and age distributions of the estimated total 967,759 have been assumed to be the same as those in this constituent sample, and have been calculated therefrom.

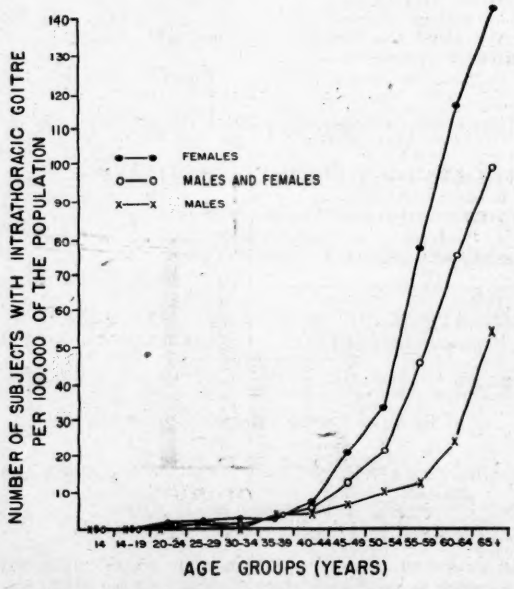

FIGURE I.

Prevalence of intrathoracic goitre in metropolitan Sydney, as shown by mass radiography. This location of goitre is characteristic of the later age groups.

A similar assumption has been made in respect of the country of origin (Table II), the distribution between the various countries of birth of the whole population being derived on a proportional basis from the known distribution in the same very large sample (192,297). The

TABLE II.

Country of Birth of Persons with Intrathoracic Goitre.

Country of Birth.	Males.		Females.		Total.	
	Number with Intrathoracic Goitre.	Number Radiologically Examined.[1]	Number with Intrathoracic Goitre.	Number Radiologically Examined.[1]	Number with Intrathoracic Goitre.	Number Radiologically Examined.[1]
Australia	19	396,410	104	394,221	123	790,631
United Kingdom, Ireland and New Zealand ..	15	46,617	22	34,695	37	81,312
Europe	8	49,139	10	19,405	18	68,544
Others	0	16,487	1	10,785	1	27,272
Not stated	4	—	11	—	15	—
Total ..	46	508,653	148	459,106	194	967,759

[1] Estimates based on known composition of a very large sample (see text).

interesting fact emerges that in persons born in British countries overseas, intrathoracic goitre as demonstrated in the surveys is three times as frequent as in native Australians and nearly twice as frequent as in European migrants (Figure II).

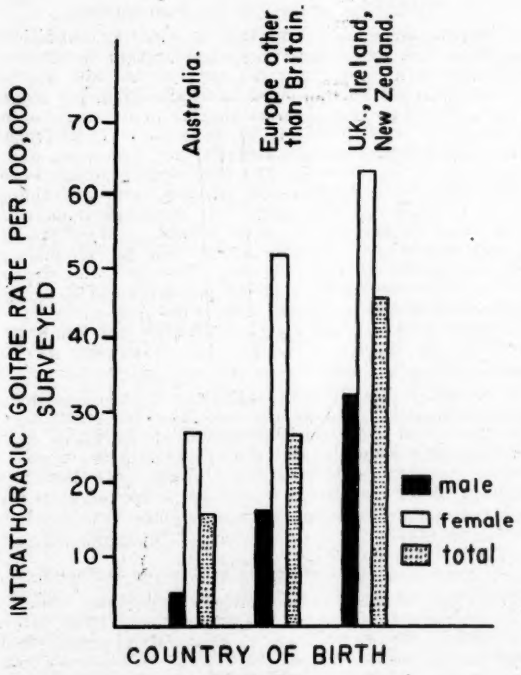

FIGURE II.

Prevalence of intrathoracic goitre revealed in metropolitan Sydney mass radiography surveys in relation to country of birth. There is a clear difference in prevalence between the three groups shown. The data in Figures I and II agree with the proposition that the goitres begin in early life, are of very long standing, and gravitate into the thorax in later years.

Discussion.

The over-all prevalence of intrathoracic goitre demonstrated radiologically in the survey was one in 5040. This may be compared with the figure of one in 753 for new and active cases of tuberculosis, and with an approximate figure of one in 3500 for cancer of the lung. Among women aged forty-five years and over, one in 2030 had an intrathoracic goitre demonstrable radiologically.

Goitre is not endemic in Sydney, as is known from surveys of school children aged five to fifteen years (Solomons, 1957), and this is in agreement with the relatively low incidence of intrathoracic goitre found in the native Australians. Among 202,554 persons who underwent mass radiography in Amsterdam, 23 substernal goitres were noted—a frequency of one in 8800 (Van Vliet, 1953). For the city of Stockholm the corresponding figure was one in 5600 (Bauer and Gentz, 1953). The Amsterdam author gives no details; but Bauer and Gentz's data are sufficient to show that in Stockholm, as in Sydney, the frequency of intrathoracic goitre increases greatly with age. It is suggested that mass surveys of cities in goitrous areas would reveal a much greater prevalence of intrathoracic goitre, and that, as public health measures, their importance would be correspondingly greater.

It is probable that in most cases the seed of intrathoracic goitre is sewn in early life—during childhood and adolescence. Its rising incidence in the later years of life, here demonstrated, is consistent with the generally accepted belief that as a group these goitres are of long standing. The data in Figure I also provide clear evidence that, whatever the causal factors are, the intrathoracic location of a goitre is characteristic of old age.

The distinctly higher frequency of intrathoracic goitre in United Kingdom migrants as compared with those from other European countries could hardly have been predicted. Our data rely only on country of birth; but this would undoubtedly be closely related to place of residence in early life. Incidentally, the marked difference in frequency among native Australians and British and European migrants strengthens the proposition that juvenile rather than current influences determine the occurrence of intrathoracic goitre.

No attempt will be made here to discuss the clinical features of intrathoracic goitre, but the significance of the present findings may be indicated briefly. In these patients intrathoracic goitre was a chance radiological finding; but careful interrogation of a representative sample (52 of the 194 accepted) revealed that less than half (23 of the 52) were truly asymptomatic. Four of the 52 had pronounced respiratory obstruction. In five patients who were symptomless, the collateral venous channels over the upper part of the thorax were conspicuously developed and engorged.

Tracheal compression and respiratory obstruction obviously comprise the chief disabilities and hazards. Cardio-respiratory disease is the commonest cause of death in elderly patients. It is precisely this group which is affected by intrathoracic goitre, and we suggest that even moderate degrees of tracheal obstruction may in old age greatly hamper pulmonary ventilation and, in the event of intercurrent respiratory infections, seriously interfere with pulmonary drainage. Clearly, the ideal to aim at is early detection and prevention of complications by surgical intervention before full descent of the goitre and advancing years constitute additional hazards.

It appears that many such goitres will be detected early only by mass radiography surveys. Even when respiratory obstruction is very severe, its true cause may be overlooked by a series of medical attendants, as in the following instructive case.

A married woman, aged forty-five years, had complained for many years of difficulty in breathing, and of feeling a lump in the throat on swallowing. At different times she had been reassured, but not radiologically examined, by three doctors. In recent months her respiratory difficulty had been increasing and was evident to members of her family. Her exercise tolerance was greatly limited. Examination of the patient revealed no palpable goitre in the neck, but respiratory stridor was obvious.

Miniature mass radiography had revealed an intrathoracic goitre, and this was confirmed by large films, the tracheal lumen being reduced to a narrow slit in the lateral view. When the patient was anæsthetized for thyroidectomy, a gum elastic bougie used as an airway was firmly "gripped" at this level. After operation she obtained immediate relief from her dyspnœa and stridor.

Summary.

1. One hundred and ninety-four cases of intrathoracic goitre have been detected among an estimated total of 967,759 different persons radiologically examined in the Sydney metropolitan area in the course of mass chest surveys between April, 1953, and December, 1956.

2. Of the intrathoracic goitre patients, 148 were women and 46 were men. In both sexes the frequency was relatively much higher in the later age groups, over 60% of patients being aged sixty years or older.

3. The frequency of intrathoracic goitre among persons born in England was approximately three times that in native Australians. Among the former also the frequency was distinctly greater than among persons born on the mainland of Europe.

4. Evidence is provided that whereas the seed of intrathoracic goitre is sown in early life, this type of goitre is of long standing and is characteristic of the later age groups.

Acknowledgement.

We wish to acknowledge the ready and able help given us by the clerical staff of the Mass Radiography Division of the Anti-Tuberculosis Association of New South Wales.

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PITFALLS IN THE TREATMENT OF ENURESIS BY AN ELECTRIC AWAKENING MACHINE.

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AND

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SINCE the work of Crosby (1950) on the control of enuresis by electric stimulation of the enuretic at the moment of micturition, increasing use has been made of this form of treatment. Whilst many favourable results have been recorded, the method cannot be regarded as a specific remedy. There are frequent failures. Our initial results confirmed the necessity for parent cooperation and personal supervision by the physician, which was stressed by Crosby. Dibden and Holmes (1955) have recently arrived at the same conclusion.

Further trial of the therapy has revealed many pitfalls in treatment. These form the basis of the present communication.

Our observations are based on 55 cases of enuresis treated by an electric apparatus which awakes the patient at the commencement of micturition. The machines employed were two "Dri-Nite" machines (one of which was lent to us by Watson Victor, Limited) and eight experimental models. In all, stimulation occurred through a faradic current which activated a buzzer and skin electrodes as described by Crosby. "Dri-Nite" type of male and female adapters were used for making the circuit.

Most of the patients have had intensive psychological testing and have been under observation for a long period. Such close association undoubtedly assists in achieving a *rapport* which is helpful to therapy and investigation. In all cases an attempt was made to maintain at least a weekly contact with the patient or relatives.

The number and variety of pitfalls encountered in the use of the stimulators explain why some patients do not achieve success in treatment. This paper is written in the hope that closer attention to detail will lessen their numbers and will help to prevent a useful form of therapy from being abandoned.

Treatment Must Not be Interrupted.

It is an elementary principle in creating conditioned responses that the stimuli must be constant in time and invariable in amount. For the enuretic the aim of treatment is to condition the child to awake when his bladder is full. Our experience shows that in home surroundings regularity of conditioning is by no means easy to procure. Some interferences are unavoidable, but others are due to ignorance and negligence. The following summary is self-explanatory: (i) Illnesses of parents, who are thereby unable to supervise treatment. (ii) Week-end trips, which necessitate leaving the machine behind. (iii) Exhausted parents, too weary to harness the child to the machine. (iv) Forgetting to turn the switch to the "on" position. (v) Intercurrent illnesses of the patient, such as measles, other epidemics or accidents. These not infrequently interrupt treatment. In one case an injection into the buttock produced so much tenderness that treatment was discontinued.

From consideration of the foregoing it would seem that parents must be told of the necessity for constancy of treatment. In those cases in which interferences can be foreseen—for example, the family's impending going on holiday, a parent's leaving for hospital, injections to be given *et cetera*—treatment should be postponed until there is a reasonable certainty of at least eight weeks' uninterrupted therapy.

Responsibilities of Parents Must be Outlined.

The use of intricate electrical apparatus entails a precision of detail which bears comparison with a surgical procedure. We are accustomed to the strict routine necessary in the preparation of patient and instruments before operation. All major procedures are initiated and performed by trained personnel. In the case of the treatment of enuresis by an electric machine, the operator is an informed parent who must carry on with a minimum of training. As the parent is ignorant alike of electrical details and elementary psychology, the need for careful briefing in the necessary technique seems obvious. It is not sufficient to give an initial "handout" of elementary information.

Parents are often confused at the time of the interview, so must be given time to ask questions in order to make themselves familiar with what is for them a complicated procedure. Furthermore, they should have ready access to the doctor as eventualities arise.

It is essential that previous therapies be discontinued, and the machine must take priority in treatment. Parents sometimes continue procedures which are inimical to the creation of the right conditioned responses. For example, they continue to awaken the child at regular intervals

whilst he is harnessed to the machine. Such a practice should cease. Equally disturbing, but not so obvious, is the very general practice of "lifting" the child before the parents retire to bed.

The following situations would not have occurred if the parents had understood their responsibilities. A statistical record of the number of mishaps is not possible, as at the commencement of this series of cases no communication of this type was envisaged. The relative frequency of occurrence is indicated by the insertion of parentheses enclosing the letter "F" followed by one to three asterisks.

1. Parents, hearing the buzz of the machine which indicates the passing of urine, do not trouble to inspect a "wet bed", though several wetting episodes may have occurred. The alternatives to be explored are: (i) whether the child could have been awakened by a stronger faradic response (F**); (ii) whether the child was awake, but too lazy to arise to the pot (F*); (iii) whether the child was sleeping so heavily that he needed medical attention to make him sleep less soundly (F***). In all cases the mother must be encouraged to give details as to whether the child awakens to the stimulus and, if not, why not. It is in order to obviate such difficulties that each patient is given the following record sheet:

NAME: DATE:

Day:	Times of Buzzing.	Bed-Dry.	Wet.	Machine Replaced?

2. The parent may neglect to see that the machine is safely anchored. In one case it had been placed on a chair and was brought to the floor by a tug on the flex. Since this episode, our invariable practice has been to warn parents to leave the machine on the ground and to provide a longer flex (F**).

3. Parents are responsible for seeing that the apparatus is clean and dry before it is used for the night. If the electrodes are wet, there is continued buzzing, which precludes treatment. Furthermore, after the child has been woken up in the normal manner by the machine, the electrodes must again be dried before being reapplied (F*).

4. Parents must determine whether the patient is being efficiently awakened by the stimulus. A record of merely "wet" is not sufficient, because the wetness of bedclothes indicates in itself that awakening has not been sufficiently early and complete. There should be the passage of only a few drops of urine before the child is awakened; this will not wet the bed. However, an exception occurred in one case, when the mother had so sealed the male sheath with "Elastoplast" that no urine could escape. Investigation showed that the electrical stimulus was too weak and an appreciable amount of urine had been passed before the child awoke (F**).

5. Parents must be warned not to delegate their authority to children. On several occasions a mother went out, leaving the apparatus in charge of an elder brother or sister. The patient thereupon refused to cooperate, and treatment was neglected (F*).

6. In every case one should discuss with the parents their availability for supervision. Sometimes they go to bed as early as 8 p.m.; this early hour gives no opportunity for ensuring the correct awakening routine. Occasionally parents sleep so soundly that they do not hear the machine (F*).

From the foregoing it is clear that meticulous care as to details is essential in this method of dealing with enuretics.

Before the commencement of treatment the parents must be briefed on details of the apparatus. Procedures and pitfalls should be clearly explained. If this recital does not dim their enthusiasm, and if there are no circumstances which preclude supervision, the use of the machine is warranted. None the less, even after this screening, some parents find the task is too difficult and evince an apathy which is inimical to success. This attitude is clearly indicated in the words of one parent, who said: "All that getting up at night! Not worth it. Rather let them wet."

The Child and the Machine.

Once the first hurdle—the correct briefing of the parent—has been surmounted, the next obstacle is reconciliation of the child to an ordeal. The prospect of being forcefully and painfully awakened is a major event. To make matters worse, the treatment introduces other psychological difficulties. Tension in the child should be avoided.

The optimum psychological atmosphere for correct conditioned responses is relaxation.

Parents sometimes predispose the child to tension and nervousness by implying that slow progress is depriving other children of the machine, or that the machine will be taken away if there is not prompt improvement.

Uncertainty is harmful and creates apprehension. Children should be accustomed to the machine by being permitted to feel stimuli of varying strengths before the actual treatment. Such familiarity dissipates fear. The demonstration should include an assurance that the stimulus will not be increased after sleep has occurred. The importance of this is that the child regards such an alteration either as a breach of trust or as an indication that the machine is unpredictable and menacing.

Very timid children may be so frightened that they awake frequently during the night, irrespective of the buzzer. In such cases conditioning to the machine does not take place. A variant of this theme is the case of the very deep sleepers who do not awake at all, either to electrical stimulation or buzzing.

One child exhibited the curious idiosyncrasy of being frightened of the buzzer, though she did not object to the faradic stimulation. The remedy was to let the child play with the buzzer button until the fear had subsided.

Curiously enough, over-enthusiasm may be detrimental.

This is shown by the case of an ambitious boy, who wished to be cured in record time. He slept so lightly in the first week that he always awoke before the buzzer. He had a week of dry nights. The parents were delighted. The following week the bed was wet every night; he slept so soundly he did not hear the buzzer.

Visitors in the house create a simple form of stress. Routines are upset, and the child feels uneasy lest they discover his enuresis.

Direct Interference by the Child.

As has already been implied, full cooperation of the child is not always possible. Several factors are responsible—for example, the negativism inherent in most children, fear of the unknown and resistance to being woken. In some cases bed-wetting is an aggressive act directed against the parents. The patient does not wish to be deprived of his secret weapon, so is naturally resistant.

The following direct interferences by the child have been noted:

1. Removal of the belt after its final adjustment by the parent is not uncommon (F**).

2. Boys frequently remove the penis sheath. (Removal of the female dagger electrode has not been noticed.) (F**.)

3. Both boys and girls have at times placed their night attire between the skin and the contact electrodes on the waist in order to prevent the electric shock (F**).

4. Two children refused to wear the belt, but consented to wear the sheath in conjunction with the buzzer. In both cases enuresis continued.

5. As might be expected, some children use the obvious method of altering the controls so as to weaken the stimulus (F*).

Mechanical Difficulties.

At the best of times, electrical gadgets are finikin. Their use in connexion with bed-wetting children must be expected to create difficulties. These are of two types—firstly the machine, and secondly the harness which connects the machine to the patient.

The Machine.

The commonest cause of difficulty with the machine is a failing battery. Often the buzzer continues to sound though the batteries have become too weak to deliver a shock via the belt. As the buzzer does not waken the child, bed-wetting occurs and there is interruption with the training until the battery fault is detected (F***). In view of the foregoing, it is essential for a parent to spring to attention whenever the buzzer sounds, and to insist upon the child's rising and passing urine.

The minimum of trouble has been due to the actual electric machines which create the faradic current. Reference has been made to the case in which the machine was pulled off the chair. Fortunately such catastrophes can be avoided.

The Harness.

Screws work loose and corrosion can occur. Both will cause buzzing without the passing of urine (F*).

A not uncommon fault is the breaking of the flex at its junction with the electrode (F**).

In boys the use of a sheath over the penis creates several difficulties. It tends to fall off, so it must be secured with "Elastoplast". Failure leads to inefficient working (F***).

The sheath is sometimes dislodged by children who are accustomed to sleep on the abdomen. Extremely restless children often dislodge the sheath and may require sedation (F*).

Some boys, on account of fear or modesty, are reluctant to wear the sheath and must be persuaded (F*).

Variation in the size of the male organ sets special problems. The extremely small variety calls for a tiny sheath. The standard size sheath may have to be cut down. Conversely, the large-sized penis may require a larger type. In one case a bicycle tube was used as a successful improvisation. There is a scope for a greater range of penile fittings (F*).

The female attachment presents fewer problems and is worn without discomfort or protest. The parents must be warned not to scrub the male rubber sheath or the female dagger insert, as often damage is done in the process. At the same time electrodes must be carefully washed after use, since erosion takes place very easily.

The most frequent difficulty was experienced through the erosion of the female electrode. This has been greatly lessened by the use of a model designed and fabricated by the staff of the Department of Physiology, University of Queensland (Figure I). They use a "Perspex" base and a simple wire electrode without fenestration. A soft rubber moulding was made, with a trough into which urine could pass. A removable plastic strip occupied the bottom of the trough, and two silver wire electrodes (two millimetres in diameter and five centimetres long) were carried by the plastic electrode holder. Cleaning is facilitated by the easy removal of this holder.

Other Hazards.

In addition to the routine difficulties already mentioned, one encounters unexpected problems. On two occasions the patient suffered skin allergy due to the "Elastoplast" webbing attaching the male sheath to the penis. It was obviated by changing the type of adhesive. In one case skin irritation occurred at the site of the belt electrodes. In accordance with the suggestion of Professor W. V. MacFarlane, a flat, chromium-plated electrode was devised. (Chromium plating was used, since nickel plating would increase the possibility of allergic sensitization.) Since this has been used there has been no more trouble.

The skin of the male organ becomes sore from repeated use of adhesives. This is apt to occur in children who wet the bed frequently and are not responding promptly to the stimulus. When it occurs, there is need for closer investigation as to waking times and general supervision of details of treatment. The sore penis can be regarded as a signpost indicating that a re-survey of the routine is necessary.

The last hazard is not uncommon. In spite of the graduated electrical shock which gives a wide range of stimulus, some enuretics sleep so profoundly that they do not waken. In these cases the remedy is not to boost the pain stimulus higher, but to lessen the sleep threshold by drugs. The following story illustrates this danger.

One child enthusiastically turned the dial to increase the shock, and the result was so terrifying to him that he was "too scared" to carry on with the treatment.

The difficulty can usually be overcome by the exhibition of amphetamine, five to fifteen grains, as necessary.

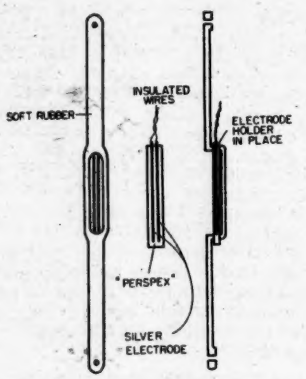

FIGURE I.

Sketch of female adapter. Full scale: measurements seven and three-quarter inches by half an inch.

Summary.

1. Difficulties occurring in the treatment of enuresis by an electric awakening machine are described.

2. The need for thorough briefing of parents is emphasized.

3. Consideration is given to the child's viewpoint.

4. Intricacies of the machine and harness are indicated.

5. Details are given of an improved type of contact button and female electrode.

Acknowledgements.

We wish to acknowledge our indebtedness to Professor W. V. Macfarlane for much help and advice in connexion with our difficulties, to Mr. H. Dakin, of the Department of Physiology, University of Queensland, for construction of the female electrode, and to Mrs. P. MacFarlane for its illustration.

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A COMPARATIVE STUDY OF ERGOMETRINE AND "METHERGIN" USED IN THE MANAGEMENT OF THE THIRD STAGE OF LABOUR.

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THE routine use of ergometrine maleate in the management of the third stage of labour was introduced at The Royal Women's Hospital, Melbourne, in 1951. This followed extensive clinical trials, in which varying doses were given by intravenous and intramuscular injection at different stages of delivery. The most satisfactory routine, and that adopted, was the intravenous injection of 0·5 milligramme of ergometrine immediately after the delivery of the baby, and an intramuscular injection of a further 0·5 milligramme after the expulsion of the placenta. During the last year, the value of "Methergin" (methylergometrine tartrate) has been assessed and compared with the results achieved by this scheme of management with ergometrine maleate.

The Conditions of the Investigation.

At this hospital only complicated and instrumental deliveries are performed by members of the honorary and resident medical staffs. In all normal cases, nearly 7000 *per annum*, the patients are delivered by pupil midwives and medical students under the direct supervision of the trained midwifery staff. Nitrous oxide (with oxygen) analgesia is used in normal births, and a pudendal block, if possible, in forceps deliveries. Caudal and general anæsthesia are used in a limited number of complicated and instrumental deliveries. As soon as the uterus contracts after delivery, an attempt is made to express the placenta by the Dublin method. Manual removal of the placenta, apart from other indications, is performed if the placenta is adherent or cannot be expelled one hour after delivery. Credé's method of expressing the placenta is seldom employed. Post-partum hæmorrhage is defined as the loss of 20 or more ounces of blood within twenty-four hours of delivery.

The Investigation.

The only patients who were excluded from this study were those delivered by Cæsarean section. "Methergin" and ergometrine were used on alternate weeks for all other deliveries throughout the period of the investigation. The giving of the drugs by random selection or to alternate patients was impracticable, and it is believed that the compromise reached, when employed in a large number of cases for a long period of time, was a satisfactory substitute. This clinical trial included more than 4000 deliveries and extended over thirty-two weeks. The dose of "Methergin", that advised by the manufacturer, was 0·2 milligramme given by intravenous injection immediately after the delivery of the baby. During the last eight weeks of the trial, this was supplemented by 0·2 milligramme given by intramuscular injection after the expression of the placenta. The scheme of administration of ergometrine, which has already been outlined, remained constant throughout the investigation.

Four aspects of the actions of these two drugs were studied. These were the rapidity with which they caused completion of the third stage, their influence on the incidence of post-partum hæmorrhage, the degree to which they affected the frequency of manual removal of the placenta, and finally their relative vasopressor properties.

The Rapidity of Completion of the Third Stage.

The rapidity of completion of the third stage is important in a busy labour ward or when there is inadequate labour ward accommodation or personnel. Ten minutes was arbitrarily chosen as the time within which the third stage should be completed. This was achieved with both drugs in nearly 87% of cases, and there was no significant difference in this aspect of their action (Table I).

The Incidence of Post-partum Hæmorrhage.

In the first twenty-four weeks, when 0·2 milligramme of "Methergin" was given by intravenous injection, the post-partum hæmorrhage rate with ergometrine was 2·2, and with "Methergin" 3·6 per 100 deliveries (Table II). In a hospital delivering 7000 patients *per annum*, this would mean that with ergometrine there would be approximately 150 and with "Methergin" approximately 250 post-partum hæmorrhages *per annum*. There was a greater number of hæmorrhages of all degrees of severity with "Methergin".

TABLE I.

Rapidity of Completion of the Third Stage.

Drug.	Number of Consecutive Cases.	Spontaneous Completion of Third Stage Under Ten Minutes.
Ergometrine ..	1000	868
"Methergin" ..	1000	865

There was no reduction in the post-partum hæmorrhage rate when an additional 0·2 milligramme of "Methergin" was given by intramuscular injection after the delivery of the placenta (Table III). This is in accord with the clinical observation that blood loss with "Methergin" usually occurred before or during the delivery of the placenta. There was a slight rise in the post-partum hæmorrhage rate associated with both drugs during this part of the trial. However, this was not significant.

TABLE II.

The Incidence of Post-partum Hæmorrhage when 0·2 Milligramme of "Methergin" was Given by Intravenous Injection Immediately After the Delivery of the Baby.

Drug.	Number of Deliveries.	Cases of Post-partum Hæmorrhage.				Post-partum Hæmorrhage Rate per 100 Deliveries
		20 to 30 Ounces.	30 to 40 Ounces.	40 Ounces or More.	Total.	
Ergometrine	1505	20	8	5	33	2·2
"Methergin"	1543	34	9	12	55	3·6

The post-partum hæmorrhage rate in the total 2031 deliveries in which ergometrine was used was 2·3 per 100 deliveries. This is identical with that found in the original trial in 1950.

TABLE III.

The Incidence of Post-partum Hæmorrhage when 0·2 Milligramme of "Methergin" was Given by Intravenous Injection After the Delivery of the Baby and a Further 0·2 Milligramme by Intramuscular Injection After the Delivery of the Placenta.

Drug.	Number of Deliveries.	Cases of Post-partum Hæmorrhage.				Post-partum Hæmorrhage Rate per 100 Deliveries.
		20 to 30 Ounces.	30 to 40 Ounces.	40 Ounces or More.	Total.	
Ergometrine	526	9	5	0	14	2·7
"Methergin"	576	17	4	4	25	4·3

The Frequency of Manual Removal.

The manual removal rate during this investigation was with ergometrine 5·6 and with "Methergin" 4·1 per 100 deliveries (Table IV). Post-partum hæmorrhage was associated with 18 cases (16%) of manual removal when ergometrine was used and with 20 (23%) when "Methergin" was given.

The greater frequency with which manual removal of the placenta was necessary with ergometrine would appear to be a reflection of its more powerful oxytocic action in the dose used in this investigation. The uterus contracts down on the placenta and prevents its expulsion.

TABLE IV.

The Frequency of Manual Removal and Associated Post-partum Hæmorrhage.

Drug.	Number of Deliveries.	Number of Manual Removals.	Number of Manual Removals Associated with Post-partum Hæmorrhage.	Manual Removal Rate per 100 Deliveries.
Ergometrine ..	2031	113	18	5·6
"Methergin" ..	2119	87	20	4·1

The Vasopressor Properties of the Two Drugs.

The blood pressure of a number of patients was recorded at frequent intervals during labour, immediately before and after delivery and then one, two and four hours later. A rise in the blood pressure within two hours of delivery of more than 20 millimetres of mercury, systolic, or more than 10 millimetres, diastolic, was accepted as significant. The blood pressure in any one case was always taken by the same person. The patients were divided into two groups, normotensive and hypertensive. The normotensive group included patients in whom there was no elevation of the blood pressure during pregnancy or labour. The hypertensive group was formed largely by patients suffering from pre-eclampsia, but there were also a small number with labile or essential hypertension.

There was a significant elevation of the blood pressure after the injection of ergometrine in four of 50 consecutive normotensive patients from whom satisfactory recordings of the blood pressure were obtained. There were no significant elevations of the blood pressure in a further 50 normotensive patients given 0·2 milligramme of "Methergin" by intravenous injection immediately after the delivery of the baby (Table V). There were eight significant elevations

TABLE V.

The Influence on the Blood Pressure of Ergometrine and "Methergin" in Normotensive Patients.

Drug.	Number of Cases.	Blood Pressure Rise of More than 20 Millimetres of Mercury, Systolic, and 10, Diastolic.
Ergometrine ..	50	4
"Methergin" ..	50	0

of the blood pressure in 50 hypertensive patients given ergometrine, and three in 50 given "Methergin" (Table VI).

It would appear, therefore, that ergometrine is more likely than "Methergin" to cause a rise in the blood pressure, and that this vasopressor property is more frequently evident in patients already suffering from hypertension. Similar conclusions have been reached by Schade (1950), by Forman and Sullivan (1952), by Carvalho *et alii* (1953), by McGinty (1956) and others. It is difficult to assess the clinical importance of this occasional vasopressor response, particularly to the injection of ergometrine. It is possible that it may be responsible for certain of the atypical cases of post-partum eclampsia and even for a cerebral vascular accident occurring immediately after delivery.

Summary.

1. The use of ergometrine and "Methergin" in the management of the third stage of labour has been studied in more than 4000 deliveries.

2. There was no significant difference in the influence of ergometrine and "Methergin" on the rapidity of completion of the third stage. This was completed with both drugs within ten minutes in nearly 87% of deliveries.

3. The post-partum hæmorrhage rate with "Methergin" was approximately 60% greater than with ergometrine. It was 2·3 per 100 deliveries with ergometrine and 3·6 per 100 deliveries with "Methergin".

TABLE VI.

The Influence on the Blood Pressure of Ergometrine and "Methergin" in Hypertensive Patients.

Drug.	Number of Cases.	Blood Pressure Rise of More than 20 Millimetres of Mercury, Systolic and 10, Diastolic.
Ergometrine ..	50	8
"Methergin" ..	50	3

4. The manual removal rate with ergometrine was nearly 40% greater than with "Methergin". It was 5·6 per 100 deliveries with ergometrine, and 4·1 per 100 deliveries with "Methergin".

5. Ergometrine more often caused a rise in blood pressure than did "Methergin". This was more frequently evident in patients already suffering from hypertension. Attention has been drawn to the possible dangers of this vasopressor action.

Acknowledgements.

I wish to express my appreciation of the cooperation and help given by members of the nursing staff. I desire to thank those medical students who aided in the recording of blood pressures, and Dr. M. S. Forrest for the results of the initial studies of ergometrine in 1950. The "Methergin" used in this study was supplied by Sandoz, Limited.

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A NON-DIRECTIVE METHOD OF GROUP PSYCHOTHERAPY.[1]

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GROUP PSYCHOTHERAPY, although a method of therapy as yet practised little in Australia, has come to stay, if one may judge from the considerable research in this direction overseas. It is therefore of considerable importance for us to consider the possibilities of this new field of therapy. It has certain attractions—firstly from the point of view of research into the effects of group tensions on individuals, and secondly in the direction of bringing therapy to greater numbers, which latter has always been an important aim of medical practice. There is also the prophylactic aspect, always of interest to medicine—namely, to what extent can suitable group therapy in young people reduce the possibilities of breakdown in later life?

[1] Read at a meeting of the Australasian Association of Psychiatrists on August 22, 1956, at Brisbane.

The task that faces the psychotherapist is to develop some system in his technique. This is difficult, because he is dealing with intangibles such as emotional states, mental attitudes and neurotic symptoms. A system of rules of procedure tends to give an undesirable rigidity to a situation which is primarily one of emotional interplay. On the other hand, a complete absence of rules means that the therapist is relying entirely on intuition, with the result that he is never sure what to say next, and that he has little idea of whether what he does say is essentially interpretation, reassurance of the patient, reassurance of himself, or defensive for his own sake. An example of the last-mentioned occurs when the therapist says something that unconsciously steers the patient away from a topic that disturbs the therapist himself.

Thus what we have to find is some systematic approach which is not too verbose, bookish and theoretical (this would only stultify the emotional aspects of therapy), and one which will, as far as possible, protect the therapist from making too many errors in the way of accidentally introducing his own unconscious problems into the situation.

It is with these principles in mind that I shall try to describe a non-directive form of group therapy, which may be of interest not only to psychotherapists, but also to those general practitioners who have a particular leaning towards psychological problems. It is from amongst the patients of a general practice, in which the widespread occurrence of minor neurotic disorder is so apparent, that really satisfactory therapeutic groups may be formed.

How far the technique here described can be extended into an analytical approach will depend on the innate capacity for insight of the therapist, and on the degree to which this has been enhanced by any analytical training he may have had.

But first let us say something about patients likely to respond to group therapy. Psychoneurotics and those with uncomplicated psychosomatic disorders are suitable. The question of having different types of psychoneurosis in the same group is not so important as it may seem from the point of view of the ultimate therapeutic result. However, research on groups comprising patients suffering from the same condition, compared with groups whose members have different clinical conditions, may throw some light on the best group arrangement for obtaining the maximum therapeutic efforts in any particular disorder.

Prepsychotics and psychotics may raise special problems. The first often show an incapacity to withstand the tensions engendered by the group, and the second often have not sufficient capacity for cooperation to attend regularly on a voluntary basis. Patients in both these categories may therefore require additional private psychotherapeutic sessions and often need some degree of supervision between sessions. There is, for instance, sometimes a danger of a schizoid patient's becoming overtly psychotic.

I should say that anything from two to eight patients constitute a group that can be worked with fairly well. As the numbers rise higher the treatment tends to become unwieldy, and provides too much opportunity for inhibited and withdrawn patients to take refuge by hiding themselves away in the "crowd".

Sessions should number two per week and should last approximately one hour each. It matters little whether the groups are of one sex or mixed, because similar problems will crop up in any sort of group. I think it important that in the early stages of treatment it should be made clear that the only complete freedom that is given in the group is in speech, and that physical contact of any sort, either in affection or in anger, is not allowed. I should like to point out here the danger of having in a group patients who are too strongly paranoid or hypomanic. In these persons the ego-control of aggression is rather precarious, and they may be relatively easily provoked to violence. Early in the treatment it should be made clear that it is expected of every member that he regard what is discussed in the group as confidential. After the preliminary introduction of the group members to one another, it should briefly be explained that they are permitted to talk about anything they like, in any way they like, and that this free discussion, together with the therapist's comments from time to time, constitutes the treatment.

This often produces nothing but an awkward silence. In this case the therapist can put into words the fact that they experience some difficulty in throwing off the usual restraints of conventional social gatherings. This is not exactly telling them anything new, for they all feel it acutely; but it clarifies the fact of this unexpected and somewhat disturbing permissiveness, and sharpens their awareness of an inner resistance against taking advantage of the freedom to talk as they wish. This, more often than not, is sufficient to lead to a discussion of the difficulties of talking freely, before others, of intimate matters.

However, it will still be some time before the group will talk sincerely of their problems. All sorts of resistances will emerge to stall off the anxiety-provoking revelations.

It is, of course, impossible in this contribution to deal in any way exhaustively with all the technical problems that occur during the course of treatment; but I shall try to give some idea of the more common, and often recurring, resistances and difficulties that will inevitably crop up and will have to be handled in some way or other. I realize that each therapist will develop his own ideas on just how to cope with these problems, and will do so largely according to his own psychological make-up. Thus, what I have to say should be regarded as rather tentative, and intended merely as a guide in what is still largely a scientific wilderness.

With regard to the chronically silent patient, the therapist should not be unduly worried about this if he is coming to the group regularly. Pointed references to his silence, however kindly, should be avoided, since obviously his unconscious anxiety is great, and he is trying to hide himself away. If he is singled out, he feels it as a signal for a group attack on him, and he may not come again. He usually takes a remark about his silence from another patient with less anxiety, and this will certainly come sooner or later. However, if there are several silent ones, the therapist can safely help by addressing them together and remarking that there must be some special difficulty here.

As far as possible, the therapist should avoid being tricked into answering a lot of questions and giving advice based on them. Sometimes it is necessary to do so, however—for example, in the instance of a person who describes symptoms and then asks if they are a sign of a certain disease. Here he can be reassured or advised to seek a medical examination. Most other questions can be dealt with most effectively by going into the patient's need to ask them. For instance, why does the patient have to ask how to deal with a difficult work mate? Why cannot he decide himself what to allow his children to do or not to do? This approach usually results in a discussion of the patients' fears, doubts and conflicts, and can often be led round to what they expect of the therapist—that he should take their responsibilities off their shoulders, that he should be a better parent than their own, and so on. If trivial talk continues for some time, the therapist should point it out, and this is usually enough to prompt somebody to bring forward a topic that means something for him emotionally. In this case we sometimes find that the others remain silent as if completely unaffected. This attitude, one finds, is defensive. When a person talks of deeply felt matters, such as grouches against spouse or parents, frustrations in his ambitions, difficulties with the opposite sex, autoerotic experiences and conflicts and so on, this always strongly affects the other members of the group despite their silence; hence their failure to express what their reactions were, and what they thought of the subject raised, can be pointed out.

An exhibitionistic, aggressive patient who monopolizes the time of the group session will eventually make some of the others impatient and restive. However, the abreaction can be helped along by asking this person why he needs to hold the floor so much, and by asking the others why they

so readily let him do so. This will often bring to light their fears of being aggressive even to the extent of standing up for their own rights. The point becomes clearer to them that they are afraid that if they give any expression at all to aggression, it may get out of hand altogether.

Group therapy in a hospital of in-patients has features which distinguish it from that with independent patients living in their own homes. It is this latter type of group work with which my remarks are mostly concerned. It seems to me that in this case it is wise to discourage social contact outside the group meetings, which, of course, is not possible with patients resident in a hospital. Social contacts outside the group tend to increase the difficulty of candid discussion inside the group, especially when mutual criticism is involved. Such contact often leads to the breaking off of treatment.

The new patient, to be introduced to a group which has already been working for some time, should be interviewed privately on a number of occasions first. This helps him to develop a good *rapport* with the therapist, which enables him to withstand the anxiety provoked in the early stages of his group experience.

You will see that I have said nothing about symbolic interpretation, and the transference. It was not intended to describe analysis in groups, but rather to discuss certain factors in a technique which might facilitate a mild continuous abreaction through talking. The therapist's task is thus seen as one in which he tries to play the part of a catalyst, keeping his own idiosyncrasies out of the picture as far as possible, and encouraging the venting of feelings on a verbal level, and the free discussion of previously prohibited topics. At least in the milder neuroses and psychosomatic disorders I think some such technique as this can produce gratifying results.

PSYCHIATRIC ASPECTS OF CHILDHOOD EPILEPSY.

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In this article I shall attempt to describe some of the more recent advances in the field of the psychiatry of infantile and juvenile epilepsy with special reference to the problem of behaviour disorders in epileptic children. This will involve a consideration of the problem of causality, which has troubled much of psychiatric thinking in a number of areas. The psychiatry of childhood epilepsy is, I believe, a good example of the insufficiency of an "either-or" concept of causality. Finally I shall discuss some recent work done at the Maudsley Hospital on juvenile epilepsy.

In order to appreciate the recent advances in the psychiatry of childhood epilepsy, one must consider the background of changing ideas concerning the classification and ætiology of the illness as a whole. Psychiatrists and psychologists continue to speak of epilepsy as a unitary entity, while neurophysiologists and neurologists have abandoned this concept and speak of the "epilepsies". As a result the two sides are often arguing at cross purposes when specific phenomenological and ætiological problems are raised.

The classification of epilepsy has undergone some radical changes in the past two or three decades. This has been due to two chief influences: (i) the ideas and writings of Hughlings Jackson on cerebral localization, (ii) the advent of clinical electroencephalography. As an extension of the latter must be mentioned the work of Penfield and his school on cerebral localization by electrical stimulation and electrocorticography in the conscious patient. As a result of these advances it is impossible to speak of epilepsy as a nosological entity; one must speak of the epilepsies (McNaughton, 1952; Penfield and Jasper, 1954).

With regard to ætiology, the term "idiopathic" has lost any justification that it may once have had, and Penfield has suggested that "cryptogenic"—that is, of unknown ætiology—may be a more logical term. He believes that all patients have a lesion or focus, even though it may be impossible to localize it with present techniques. His term "centrencephalic" has no ætiological connotation, but merely indicates the mode of spread of the discharge through the diencephalon and the thalamo-cortical systems. However, some authors—for example, Lennox—would maintain that some cases have a purely genetic ætiology and speak of "genogenic epilepsy".

To turn now to childhood epilepsy: one of the terminological difficulties has been the distinction drawn between infantile convulsions and epilepsy, the former having a supposedly better prognosis. According to modern neurophysiological thought, there is no justification for making this distinction. Once epilepsy is defined as a "spontaneous, self-sustained, hypersynchronous discharge of nerve impulses of high frequency spreading synaptically and ephaptically" (Gastaut, 1954), infantile convulsions must fall under the same heading. The ætiology of so-called febrile convulsions is variable; in some cases there is a preexisting atrophic lesion which discharges only when the patient is febrile; in others the febrile illness is meningitis or meningo-encephalitis which provides the focus; and in a few there is a genogenic epilepsy which becomes clinically manifest only with fever. As might be expected from such a mixed group, the prognosis is not uniformly favourable. The estimated incidence of epilepsy in later life varies in different series from 6·5% (Melin) to 20% (Zellweger).

There are other physiological precipitating factors in children, such as low blood calcium content and hypoglycæmia, but they are of small importance. Peterman (1946) gives an incidence of 7% for the former; but in the experience of other authors tetany plays a part in a much smaller percentage of cases.

It can be seen, therefore, that physiological factors are all too often absent, and the pathological anatomy is rarely sufficiently known for either factor to provide a satisfactory basis for classification. The electroencephalographic evidence, on the other hand, will throw light on at least the method of spread of the discharge, even if it fails to localize its site of origin. With methods of activation, of which over-breathing, photic stimulation and barbiturate sleep are the most useful and practicable in children, an epileptic discharge can be produced in over 80% of cases (Nuffield, 1956). Its precise localization may be more difficult in children than in adults. This is particularly the case in deep temporal, orbital and medial surface lesions. Many bilaterally synchronous generalized discharges have such an origin, and one must be careful to distinguish them from primarily centrencephalic cases. In the latter, lesions may also be present; but, if so, they are subcortical ones in the diencephalon or brain stem. The features that make one suspect that a given subcortical discharge is a secondary phenomenon are: (i) uneven distribution and (ii) irregular wave form. The latter is of particular importance, as the clinical correlates of the spike and wave phenomenon are more varied than the original work of Lennox and Markham (1953) and of Gibbs *et alii* (1954) suggested (Silverman, 1954; Knott and Clark, 1955; Hill, 1956*b*). I have dwelt on the finer points of the epileptic discharge because they are also important from the characterological point of view, as I hope to show later on.

One of the most benighted concepts of the psychiatrist is that of the "epileptic personality", a term first used by McCurdy in 1916, and much time has been spent arguing for or against the existence of this entity. Indeed, this heuristically sterile battle still rages strongly in the German literature to the present day, when the issue of the "*epileptische Wesensveränderung*" is by no means dead. Strotzka (1955) divides authors on the epileptic character change into the following four groups: (*a*) those who believe in the personality change on an hereditary, constitutional basis (German school of Stauder); (*b*) those

who deny the existence of the personality change and consider epilepsy to be a psychosomatic entity (some American authors); (*c*) those who consider that the condition arises out of a particular variety of epilepsy (British school of Pond *et alii*); (*d*) those who believe that the character change is a rare phenomenon and arises out of a variety of organic and (more commonly) environmental factors. This summary of Strotzka's gives a good bird's eye view of the various schools of thought on the subject. It can be seen, moreover, that only in the British group is there any reference to the classificatory problem and the varieties of epilepsy.

The German school is somewhat archaic and nowadays largely discredited, though a number of French authors seem to have very similar ideas (for example, Rondepierre, 1951). It has a long and venerable history; but nowadays its chief importance lies in its effect of therapeutic nihilism and a tendency to stigmatize the sufferer in the eyes of the community. In the past, various pieces of repressive legislation have been one of its fruits (for example, the Swedish law of 1758 forbidding the marriage of epileptics); but they have been singularly ineffective in lowering the incidence of epilepsy (*vide* Alström, 1950). Descriptions of certain epileptic states with psychiatric features, beginning with that of epileptic furor by Esquirol in 1827 (Temkin, 1945), have led to an association between epilepsy and mental abnormality and crime in the popular mind. This trend has only quite recently become reversed, largely owing to the effect of propaganda by such bodies as the American League against Epilepsy, the British Epilepsy Association *et cetera*.

Emotional Precipitation of Attacks.

A good deal of the psychiatric literature on childhood epilepsy deals with emotional precipitation of attacks. Much of it is frankly anecdotal and consists of the description of a very small number of patients, generally evoking the plea for greater recognition of emotional factors. The significance of the attack itself is variously interpreted by analytical authors (Heilbrunn, 1950); but this need not concern us here. The beneficial effects of psychotherapy are illustrated by the case material (Sperling, 1953; Gottschalk, 1953). Of special interest in this connexion is the work of Barker, Burgwin and Simons (1950) on the experimental precipitation under "Sodium Amytal" of paroxysmal electroencephalographic abnormalities with or without clinical *petit mal* by the discussion of emotionally significant material. More recently Gastaut has made the showing of an emotionally significant film to the patient into a standardized activating technique. All psychoanalytical papers suffer from the defect of an inadequate classification, and they tend to draw conclusions from too small a number of specially selected patients (for example, Kaye, 1951). The latter may be unavoidable; but the former is more serious, as it ignores recent advances in this field. As Kubie (1953) has pointed out in the adult field, it would be necessary to analyse a series of Penfield's cases before one could work out precise relationships between psychopathology and neurophysiology in epileptics.

The Petit Mal Child.

Looking through the psychoanalytical literature, one is struck by the fact that the majority of papers describe cases of clinical *petit mal*. This may be a particularly "psycho-labile" form of discharge, when one remembers how easily it is provoked by physiological activation, especially hyperventilation (though sleep, natural or barbiturate-induced, tends to suppress it).

As long ago as 1906, Friedman drew attention to the peculiar psychological traits of the *petit mal* child. He described these children as "affectated and emotionally labile", and considered the attack to be an hysterical phenomenon in the nature of a "death feigning reflex", thus anticipating some of the later psychoanalytical literature (for example, Jelliffe and White, 1935). More recently a paper by Siegmund and Pache (1953) separated two psychologically distinct groups of *petit mal* children. The method used was the Bero test, a modification of the Rorschach test. One group showed "neurotic" signs, such as labile affect, basic anxiety; the other exhibited "ictophil" signs, such as perseveration. The first group responded well to "Tridione" and tended to have a remission during adolescence; the latter group showed little response to "Tridione", and a number of patients developed *grand mal* on gaining maturity. One suspects that the authors are dealing with two physiologically distinct groups of patients, and that the second group would have atypical electroencephalographic findings, such as irregular spike and wave; but the authors do not give any electroencephalographic data.

Pond (1952), describing his first 150 cases, found among them a group of *petit mal* children of characteristic physical appearance and character traits: fair, blue-eyed boys, and dark-haired, rather untidy girls. Both sexes were serious, nicely mannered, rather passive children, who might be stubborn, but rarely showed much overt aggression. The personality contrasted with that of the *grand mal* group, with brain injury but normal intelligence. The latter were more aggressive, and the social situation also tended to be worse. Since Pond's original article, quantitative studies have confirmed his impressions of the passive, "neurotic" nature of the *petit mal* child (Nuffield, 1956).

Other Subvarieties of Juvenile Epilepsy.

Apart from the two groups of epileptic children already mentioned, Pond (1952) also described two groups of mentally defective epileptic children: (*a*) a static group, in which mental defect and epilepsy are both due to severe brain injury; (*b*) a dynamic group, in which there is progressive deterioration, with frequent *grand mal*, *status epilepticus* and confusional episodes punctuating the course of the illness. Pond and Bidwell (1954) described a number of cases of *petit mal* status (*petit mal* automatism of Penfield and Jasper). The condition is often clinically mistaken for hysteria, but the electrophysiology is typical—prolonged bursts of three per second spike and wave pattern—and must be distinguished from automatism of temporal lobe origin (Tucker and Foster, 1950). The prognosis is generally good, and mental deterioration is not to be expected.

A rare but clear-cut condition is that of hypsarrhythmia (Gibbs, Fleming and Gibbs, 1954) or "*Blitz-, Nick-, und Salaamkrämpfe*" (Hess and Neuhaus, 1952). The onset is nearly always before the age of five years (when *petit mal* is rare), and most of the children are mentally retarded. Hess and Neuhaus distinguish between congenital and acquired forms. According to Gibbs, Fleming and Gibbs, who have collected a large series of cases (237), 11% of patients die in the first year of illness. These workers reported some response to "Phenurone" and also to a combination of some of the newer antibiotics ("Aureomycin", chloramphenicol, "Terramycin").

Another distinctive group is that of the hyperkinetic epileptic children, of whom Ounsted has recently described a series (1955). These children exhibit a restless aggressiveness of such severity as to be virtually uncontrollable. A parental over-protective attitude is said to be characteristic; Ounsted has called this "hyperpædophilia". He has found "Mysoline" the most useful anticonvulsant in this subvariety.

Finally I must mention the children with self-induced photogenic attacks (Robertson, 1954). I am not aware of any detailed psychological analysis of these cases. Robertson recommends superficial psychotherapy—explanation and persuasion; psychiatrists would probably prescribe anticonvulsants, but these are of very limited use in this condition. Characterologically, the patients I have observed have been passive and withdrawn, closely resembling the *petit mal* group.

Behaviour Disorders in Epileptic Children.

Behaviour disorders are probably the most important psychiatric aspect of juvenile epilepsy and need to be discussed in some detail. Considering the vagueness of the criteria of what constitutes a behaviour disorder, it is a

surprising fact that there is a considerable degree of agreement concerning the gross incidence of these disturbances in epileptic children.

Estimates vary from 9% (Bridge) to 12% (Henderson). However, Bridge (1949), in his classical work on childhood epilepsy, states that while only 9% have a serious personality disorder, 37% are mildly disturbed, and that these figures might have been higher had the earlier cases of the series been studied as intensively as the later ones. It is impossible to gauge the true incidence of psychiatric disorder in epileptic children from the study of two or three series, as the figure will vary according to the source of the cases and the function of the clinic. Certainly there appears to be some agreement among the workers in this field that every type of behaviour disorder known to child psychiatry may appear in epileptic children, and that there is little or nothing that is specific about the behavioural symptoms. That is certainly Bridge's point of view.

Bridge gives the incidence of the various behavioural disturbances in his series, but unfortunately his classification is rather untidy and could be improved. Two of his headings—for example, insecurity reaction and "spoilt child" reaction—illustrate that he is confusing phenomenology and ætiology, and the exact nature of the child's behaviour does not emerge clearly from his description. Apart from this, some organization of the material would appear desirable. This could be done in terms of underlying personality traits, yielding two or three variables; but Bridge has contented himself with simple descriptions of the behavioural symptoms.

In dealing with the environmental data, Bridge allots to each case a rating on a five-point scale of increasing adversity. Then, taking only the cases in the two highest groups, he analyses the nature of the adverse environmental situation. This yields a heterogeneous group of 11 situations, some quite specific (for example, parental alcoholism), others vague (for example, unsatisfactory home setting), and others again on different planes of causality (for example, family incompetence and irresponsibility; unsatisfactory habit training—the latter may be due to the former).

When Bridge comes to examine the correlation between the personality and environmental factors, he naturally finds it to be very high ($r = +0{\cdot}79$). He does not believe that emotional disturbance can be the sole cause of epileptic attacks, but that they may aggravate the condition as an additional factor (as illustrated in Gibbs's "Science and Seizures"). The personality or behaviour disorder is the expression of the child's reaction to the total situation—a formulation that is in accordance with a Meyerian approach; and the epilepsy itself is an important landmark in the life situation. Bridge is impressed by the importance of fear of seizures, though his figures hardly bear this out—eight cases out of 742. This train of thought is somato-psychic—that is, the effect of a physical condition on the psychological and social health of the individual.

This is also the approach of the Boston school (*vide* Lennox and Markham, 1953) and of some French authors (Michaux, 1953). Lennox has for some time been interested in the social effects of epilepsy, and has taken a leading part in propaganda emphasizing the respectability of the condition. Nevertheless, much folk-lore is still active in the mind of the parents of epileptic children, as psychiatric workers dealing with them can testify (*vide* Bidwell, 1952).

A more detailed study of maternal attitudes has been undertaken by Strotzka and his co-workers, and this appears to be the focal point of interest of the Vienna school. Apart from a high incidence of neurotic maladjustment in the mothers, the significance of which cannot be assessed in the absence of controls (Werbenjak and Strotzka, 1953), the chief point of interest lies in the paper of Navratil and Strotzka (1954) on the incidence of rejecting attitudes in Kanner's sense: (i) open hostility, (ii) perfectionism, (iii) compensatory over-protection. Having constructed a *questionnaire* to gauge these factors, they find that anxiety, guilt and over-protection emerge much more frequently than hostility and overt rejection. The significance of these findings is somewhat impaired by the fact that the controls (mothers of children left in day shelters) are probably loaded in favour of hostility and rejection. This the authors themselves admit. Although Strotzka and his co-workers state that one must not group all epileptics together, they have done so in their studies of maternal attitudes, and no intra-group comparisons are available. Nevertheless, Hoff (1953) is inclined to believe that the epileptic character change (*"epileptische Wesensveränderung"*), the nature and cause of which has been so hotly debated in the German literature, is as a rule the outcome of the mother's neurotic attitude. This view is diametrically opposed to that of most German authors, who would regard it as an organic process (Stauder, 1938).

This either-or dilemma—organic or psychogenic—which is prevalent throughout the whole psychiatric field can be pursued into the byway of epileptic behaviour symptoms, where we find Bradley (1951) splitting the phenomena into primary and secondary behaviour disorders, the former the result of cerebral dysfunction, the latter the reaction to a chronic illness. The former group comprises: (i) erratic variability in mood and behaviour, (ii) hypermotility, (iii) irritability, (iv) short, vacillating attention span, (v) selective difficulty in mathematics. Hostility, fear and despair are secondary symptoms. As Bradley admitted, the former group are signs of brain damage, the exact localization of which is somewhat obscure. Hypermotility and shortened attention span recall the cases described by Ounsted. It is plainly unsatisfactory to consider these "organic" signs as specifically epileptic, when the structural basis of epilepsy permits of wide variations. Furthermore, as Pond (1952) has pointed out, every symptom has a physiological basis as well as a psychological significance, and this renders the division into organic (or primary) and psychogenic (or secondary) entities meaningless.

An entirely different view is taken by Peterman (1953), who regards temporal lobe epilepsy or "the thalamic syndrome" as a well-established clinical entity (thanks to the Gibbs), and who considers that a specific behaviour disorder is part of the condition. If the epilepsy is of some other variety, the behaviour disorder cannot be ascribed to it. He quotes a series of 19 children with temporal lobe spikes who have all sorts of psychiatric symptoms, ranging from "nervousness" to being uncontrollable. There is some attempt here to correlate neurophysiological factors with behavioural disturbance, but the latter is not classified or organized in any way. Nor is there any mention of the quality of the environment. Pond has mentioned that in many cases of temporal lobe epilepsy the environment appears to have been particularly unfavourable, and that this, as much as the epilepsy, seems to have brought forth a severe behaviour disorder.

Recent Work at the Maudsley Hospital.

The Maudsley Hospital clinic for epileptic children has already been described by Pond (1952) and by Pond and Bidwell (1954). Its special feature is the provision of full electroencephalographic and child guidance facilities for these children; hence patients are referred to it from a wide variety of sources, not only from general practitioners, but also from other child guidance clinics who lack electroencephalographic facilities, and pædiatricians who do not have access to a full psychiatric team. Only about 50% of the patients referred turn out to be epileptic, as many are referred for electroencephalographic examination in the absence of clinical epilepsy when an organic background to their behaviour disorder is suspected, or simply in the presence of a family history of epilepsy. Over the years an impression has been gained that environmental factors are of paramount importance in the causation of disturbed behaviour—rarely have gross disturbances in the environment been absent in the case of severe behaviour problems. Furthermore, practically every type of behaviour disorder known to child psychiatry has been found in epileptic children.

In a recent study Grunberg and Pond (1957) attempted to find out in detail what environmental factors were the

most relevant. From the Maudsley Hospital item sheet they ascertained the incidence of the following factors: (i) disturbed maternal attitude, (ii) disturbed paternal attitude, (iii) epilepsy, psychosis, neurosis or psychopathy in parents, siblings, or parents' siblings, (iv) sibling rivalry, (v) marital disharmony, (vi) excessive restrictiveness, (vii) breaks and changes in environment. Groups of epileptic children with and without behaviour disorders were matched for sex and age, and the difference in incidence was submitted to statistical analysis. Factors (i) and (vii) proved to be significantly different at the 0·1% level. A disturbed maternal attitude was one of over-protection, of solicitousness or of excessive hostility, rejection, lack of concern. The relative incidence of these could not be ascertained from the data. Breaks and changes in the environment meant the child's being frequently moved from one household to another, or the family's making frequent moves. Many, but not all, children in institutions would fall under this heading. Differences between the two groups in the incidence of marital disharmony and excessive restrictiveness were significant at the 2% level, disturbed parental attitude at the 5% level. Sibling rivalry and the family history showed no significant differences.

The authors also matched a group of disturbed epileptic children with a group of disturbed non-epileptic children (the latter including only those who had normal electroencephalograms), and compared the environmental factors operating in these patients. No significant differences were found. They concluded that the environment was of paramount importance in the production of behaviour disorders in epileptic children.

It then remained to be seen what part, if any, the neurophysiological factor played in these disturbances, and whether the type of the behaviour disorder was in any way related to the electrophysiology of the subject as shown in his electroencephalogram. Bearing in mind Pond's description of the personality characteristics of *petit mal* and *grand mal* children, the author investigated this problem by a perusal of all the data available from the years 1947 to 1955 inclusive. This work is described in full detail elsewhere (Nuffield, 1956). Its most striking findings were the aggressivity of children with temporal lobe foci, and the lack of aggression in true *petit mal*—that is, those with a three per second spike and wave pattern. Only by sharply separating the three per second spike and wave group from an irregular spike and wave group could those characterological differences be clearly demonstrated. The latter were intermediate between temporal lobe and true *petit mal* children in their aggressivity. It could also be shown that so-called neurotic features in children—namely, fears, anxiety attacks, excessive timidity—were greatly diminished in temporal lobe children, but enhanced in the three per second spike and wave group. All the "experimental" groups were compared, not only with one another, but with a so-called "control" group, consisting of epileptic children with non-temporal cortical foci. It was postulated that there were at least two brain systems involved, leading to fundamentally different behaviour—the rhinencephalic and centrencephalic. As is already well known from animal experiments (Klüver and Bucy, 1939), removal of the former tends to diminish aggressive behaviour; less familiar is the hypothesis that involvement of the centrencephalic system predisposes the subject to neurotic manifestations. In either case an environmental stimulus appears necessary to set off the disturbance. This schema is, of course, not intended to be an explanation of the ictus, but only of the interictal events. To put it another way, if the "why" of the epileptic's abnormal behaviour lies in the environment, the "how" appears to be determined by the neurophysiological status.

Conclusion.

The subject of juvenile epilepsy is of interest to a number of branches of medicine—pædiatrics, neurology, neurophysiology, and finally psychiatry. In the past the contributions of the psychiatrist have merely reflected his isolation from the main body of medicine; but in recent years he has become more aware of the developments in the other branches, especially neurophysiology. Electroencephalography has become an indispensable aid, although too many psychiatrists still expect it to solve all their diagnostic puzzles, instead of treating it as an instrument of research (Hill, 1956*a*). Finally, I should like to reiterate my objection to the either-or concept of causality—is it organic, is it psychogenic? These two sets of factors are always present, but they do not act in an additive fashion. There are pathogenic and pathoplastic factors (Mayer-Gross), and in the behaviour disorders of childhood epilepsy the former are environmental, the latter physiological.

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THE NATURE OF THE ALLERGIC REACTION IN THE MAMMALIA.[1]

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FROM an historical point of view the principles of allergic reaction were all laid down between 1900 and 1910. The classical experiment on dogs by Charles Richet is well worth quoting in its entirety:

> During a cruise on Prince Albert of Monaco's yacht, the Prince and G. Richard suggested to P. Portier and myself a study of the toxic properties of the Physalia found in the South Seas. On board the Prince's yacht experiments were carried out, proving that an aqueous glycerin extract of the filaments of Physalia is extremely toxic to ducks and rabbits. On returning to France, I could not obtain any Physalia and decided to study comparatively the tentacles of actinaria, which resemble Physalia in certain respects and are easily procurable. Owing to the kindness of Y. Delage, I was able to obtain a large quantity; the tentacles cut close to the body were placed in glycerin and thus we had in Paris several litres of an intensely toxic fluid, the glycerin dissolving and extracting the active principle. While endeavouring to determine its toxic dose, we soon discovered that some days must elapse before fixing it, for several dogs did not die until the fourth or fifth day or even later after administration. We kept those which had been given a dose insufficient to kill, in order to carry out a second investigation upon them when they had completely recovered. At this point an unforeseen event occurred. The dogs which had recovered were intensely sensitive and died a few minutes after the administration of subsequent small doses.
>
> The most typical experiment, that in which the result was indisputable, was carried out on a particularly healthy dog named "Neptune". He was given at first 0·1 cc. of the glycerin extract without becoming ill: twenty days later as he was in perfect health, I gave a second injection of the same amount. In a few seconds he was extremely ill: breathing became difficult, and he was panting. He could scarcely drag himself along, lay on his side, was seized with diarrhœa, vomited blood, sensibility diminished, and he died in twenty-five minutes.

This, to all outward respects, would appear to be a typical case of anaphylaxis; but as Ratner points out, it is surprising that Richet actually discovered anaphylaxis in a dog, as it is extremely difficult to induce anaphylaxis in a dog. At the time it was thought that the reaction was due to "toxic accumulation"; but as it was shown that it could occur two to three weeks after the first injection, this excluded the cumulative concept. D. A. Prentice (1955) has recently described those cutaneous sensitivity reactions which were discovered during the intense wave of interest which permeated the early part of this century and given the names of their discoverers, so it is unnecessary to go into this aspect.

Anaphylaxis in Animals.

As the various animals react by a different sequence of events to the entrance of foreign protein, it is considered advisable to try to sort out these reactions for the following reasons: (*a*) Human beings can show a counterpart to these reactions which occur in animals. (*b*) The different reactions of different animals point a way to the possibility that different factors or organs may be involved, and thus we may be better informed of the basic nature.

As you well know, the clinical picture will be influenced by, and modified by, the degree of sensitization, the amount of the antigen and the mode of its introduction. The factors having the greatest influence on the condition of anaphylaxis are the following: (i) the species of animal, (ii) race, (iii) age, (iv) diet, (v) endocrine function, (vi) temperature.

Guinea-Pig Anaphylaxis.

The characteristic feature of anaphylaxis in the guinea-pig is the result of spasm or stenosis of the bronchioles, which produces asphyxia, convulsions and widespread pulmonary emphysema. This is preceded by severe itching of the muzzle, ears and paws, with bristling of the fur. From the emphysema *et cetera*, death frequently occurs in the acute form of reaction, whilst in the protracted form dyspnœa and anoxic symptoms occur from lobular emphysema. At autopsy the lungs are completely ballooned out with trapped air, owing to stenosis of the bronchioles and dilatation of the alveoli.

It has been shown that if the guinea-pigs are kept at 6° C. they fail to become sensitive to sheep's serum, whereas controls kept at 17° to 21° C. are highly sensitive. Similarly, artificially induced fever will protect them. Another curious factor is that older guinea-pigs are more readily protected than young ones.

Canine Anaphylaxis.

The clinical picture of canine anaphylaxis has already been depicted in Charles Richet's classic description. The major characteristic symptoms are due to the pronounced stenosis of the hepatic venules, which are well endowed with unstriped muscles. There is considerable engorgement of the liver with blood, and also in association considerable engorgement of the splanchnic vessels, associated generally with a profound and progressive fall in arterial blood pressure. Thus by damming of the blood in the hepatic and splanchnic region, the animal becomes exsanguinated into these systems and dies from anæmia of the central nervous system.

Rabbit Anaphylaxis.

In rabbit anaphylaxis there is none of the extreme dyspnœa seen in the guinea-pig; but the major effects occur from a contraction of the pulmonary arterioles in the lesser pulmonary circulation, which is followed by a fall in arterial blood pressure and slowing of the heart. The right ventricle may be so distended as to become paper-thin. There is no evidence of any bronchial obstruction and the lungs are found to be deflated at autopsy.

[1] Read at the annual meeting of the Australian Society of Allergists on November 9, 1956, at Melbourne.

Horse and Cattle Anaphylaxis.

In horse and cattle anaphylaxis, the three outstanding signs are, firstly, dyspnœa in association with wheezing and rales, which can be heard at some distance from the animal. This is followed shortly afterwards by signs of increased peristalsis with at first the passage of solid fæces and then of watery fæces in association with abdominal cramps. As the reaction increases in severity the third symptom is evident; sweating occurs, and sweat pours from the animal in rivulets. After repeated injections these symptoms are associated with itching urticaria and œdema of the skin, with congestion and swelling of the mucous membranes.

Monkey Anaphylaxis.

Monkey anaphylaxis has been found difficult to induce, and when it occurs it may take up to twenty-four hours to be complete. The severe reactions are usually characterized by dyspnœa, weakness, salivation, vomiting and extreme discomfort, causing the animal to roll over. On post-mortem examination there are variable findings, such as petechial hæmorrhages of the lung, accompanied by emphysema, hæmorrhage and œdema of the intestinal tract and abdominal viscera. These are associated with pronounced dilatation of all chambers of the heart and distension of the stomach.

Cat Anaphylaxis.

Cat anaphylaxis is not so well documented as that in other animals; but it would appear that the main impact is on the gastro-intestinal tract, with increased intra-intestinal pressure and a fall in blood pressure and in temperature. At the same time the kidney volume is decreased owing to spasm of the renal arteries.

Anaphylaxis in Man.

Man shows a combination of these various types of reaction. Probably the guinea-pig type is observed more frequently than others. The protracted form of guinea-pig anaphylaxis is paralleled by bronchial asthma. The canine form would appear to occur in cases of sudden and fatal shock—for example, penicillin reactions of the acute type. The cattle type is seen in cases of angioneurotic œdema and urticaria. It is suggested that the rabbit type may occur in the little-understood cases of aberrant findings in the electrocardiogram.

The reason for the combination of the various different types of anaphylaxis in man can be explained by the fact that man, in contrast with animals, has a number of shock organs, whilst in animals all members of the same species respond with the same clinical manifestations. Hence the change in allergic states in man with advancing age.

Mechanism of Anaphylaxis.

By this review of the various mechanisms in different animals and in man it has been shown that all these symptoms are due to an antigen-antibody reaction, which occurs on the smooth (unstriped) muscles, in the mucous membranes, and/or in the capillary endothelium.

The smooth-muscle reaction takes the form of spasm. This can be seen in bristling of the animal's coat, to take one example, or in bronchial spasm and gastro-intestinal cramps.

The reaction in mucous membrane takes the form of œdema and gelatinization of the mucous membranes—for example, œdema of the conjunctivæ in the severe form of hay-fever.

The reaction in the capillary endothelium is second in importance to the smooth-muscle reaction, and takes the form of changes in calibre; with changes in permeability it leads to œdema and diapedesis. It is interesting that this generalized capillary hyperpermeability seen in the anaphylactic reaction occurs in the numerous species of animals as well as in man.

It has been shown by numerous experiments that the antigen-antibody reaction takes place in the cells themselves, and not in the circulation. Perhaps the better known of these experiments are the following: (*a*) Replacement of 98·5% of normal blood will give rise to a typical reaction with introduction of the antigen if the animal is presensitized. (*b*) Replacement of the blood of a sensitized animal with normal blood will be followed by the subsequent production of a typical reaction for that species of animal. (*c*) The production of the typical animal response in bloodless, denervated, isolated, sensitized organs will occur on exhibition of the antigen.

The necessary presence of unstriped muscles in large quantities in the shock organs of various animals has been strikingly demonstrated by experiments. Thus Simonds found in the dog that changes in blood pressure with hepatic and splanchnic engorgement were the direct result of spasm of the muscles of the hepatic venules with stenosis. Since then Thomas and Essex have demonstrated this in their studies of hepatic veins with injections of vinyl acetate.

Similarly in the rabbit, in which the main shock organ is the lung, with the pulmonary arterioles in spasm it has been shown by Boquet, Dvoretsky and Essex with different coloured plastics that the pulmonary veins could be filled completely; but on the arterial side the plastic could not penetrate beyond the larger arterioles.

In man there is a large amount of unstriped muscle around the central adrenal veins, and as long ago as 1921 Gideon Wells postulated that this fact indicated a probable association of the adrenals with the allergic reaction. Since the discovery of cortisone and other adrenal compounds we have been amazed by some of the striking effects which they have produced in allergic states; but as far as I can find out, no investigation has yet been able to give a suggested mode of action of these compounds.

Theories of the Causation of Allergic Reaction.

Histamine Theory.

The histamine theory is too well known to be dealt with here in its entirety. Suffice it to say that it is based on Lewis's triple response: (*a*) local vasodilatation of capillaries by direct action—blanching; (*b*) widespread dilatation of outlying venules and arterioles rising from a local nervous reflex—reddening; (*c*) increase in the permeability of the minute vessels by direct action, which leads to œdema.

This is considered to be due to an "H" substance similar to histamine. However, a drop in temperature and prolongation of the coagulation time of the blood are absent in histamine shock. It is considered by some that these are substances which are involved in the allergic reaction to a greater or less degree. For instance, Code has found that in certain species histamine, instead of being increased during and immediately after a reaction, was reduced. French investigators such as Vallery-Radot (1931), Villaret and others are of the opinion that allergic states are the result of excess of acetylcholine or of some disturbance in the normal breakdown by the choline esterases. They, like others also, point to the fact that certain allergic patients show signs of overaction of choline, such as excessive sweating, salivation, dyspepsia of the hyperacidity type, spastic colon and dermographism. In order to correlate these two points of view, Wittich has advanced a theory in which both choline and histamine are involved, by means of a nervous reaction in the cell.

By all these experiments and their results we are led, as Urbach was, to the conclusion that these substances, histamine and choline, are purely the end products of the allergic reaction, and are not its activators or mediators.

Arteriolar Spasm Theory.

It was the position as stated in the previous paragraph that led others, such as Simonds and Ratner, to postulate the arteriolar spasm theory—that the initial action is directly on the unstriped muscle. Ratner believes the mode of progression to be as follows: (*a*) sudden constriction of arterioles by contraction of unstriped muscles resulting in arteriolar pressure—blanching; (*b*) stoppage of blood to the venules with sudden back-flow—reddening; (*c*) increased pressure on the endothelial linings of the venules and lymph structures with transudation into the surrounding tissues—œdema and weal formation.

This direct action on unstriped muscle would explain why in an acute allergic reaction in man, who has a large number of shock organs, the whole body is involved in the reaction because all the unstriped muscle is involved.

Abell and Shink (1935) were able to demonstrate the behaviour of arterioles, capillaries and venules in a rabbit during anaphylaxis. There was arteriolar contraction caused by spasm of its unstriped muscle, and no contraction of the capillaries and venules. It has been considered that this theory does not take into account the exudation of fluid which occurs; but Ratner has explained this by referring to the gradients of pressure in the various capillaries, venules and arterioles. Possibly it is this part of the reaction which is caused by histamine produced as a by-product.

Other Theories.

Before I go briefly into any of the other theories, it is interesting to note that when Feldberg was recently investigating the reaction to a nettle sting, it was thought that the actual pain was due to histamine. This was found not to be so, so acetylcholine was considered to be the offender. Again this was found "not guilty", and eventually a third substance, hydroxytryptamine, was found to be the offender.

The Physical Theory.—The physical theory has as its principal champion Doerr. He assumes that the antigen and antibodies of great molecular weight react in the cell membrane and cannot penetrate into the cell; physiochemical changes take place, and act as irritants to the cells, which serve to upset the delicate adjustment of the colloidal conditions existing in the blood as well as at the surfaces of the cell.

The Colloidal Theory.—Widal looks on anaphylactic shock as representing a disturbance of the colloidal balance.

The Flocculation Theory.—Lumière explains the reaction as being in the nature of invisible flocculation occurring in the blood-stream.

Conclusion.

Thus we have a number of theories which have been advanced to explain the allergic reaction. It would appear that only two are at all feasible—(*a*) the histamine theory (histamine either by itself or in association with acetylcholine), (*b*) the arteriolar spasm theory. To my way of thinking, the latter theory appears to be the more reasonable. Particularly is this so when one encounters the poor results obtained with antihistaminics in certain conditions such as bronchial asthma, in which the shock organ is rich in histamine; yet there is virtually no effect with most, if not all, of them.

Summary.

1. The mechanisms of anaphylaxis in different species of animals are compared and contrasted, amongst the animals themselves and with those in man. The antigen-antibody reaction is considered to be the mechanism involved.

2. The various theories of anaphylaxis are described, the two principal theories are compared, and the advantages of the arteriolar spasm theory are put forward to support the contention that this is the more likely one of the two.

3. The relative ineffectiveness and inefficiency of most antihistaminics are considered to be due to their acting on the by-products of the antigen-antibody reaction and not on the reaction itself.

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GEORGE EDWARD TWYNAM (1856–1941), OF SYDNEY: DECOMPRESSION DISEASE OF BONE.

By MICHAEL KELLY,
Melbourne.

DECOMPRESSION necrosis of bone, according to Kahlstrom, Burton and Phemister (1939), was first described by G. E. Twynam (1888*a*) in the *British Medical Journal*. When I consulted the article I was surprised to find that it came from Sydney. The patient had been exhibited at a meeting of the medical section of the Royal Society of New South Wales by Twynam, who was an assistant honorary surgeon at Prince Alfred Hospital.

The patient, after working in March, 1882, at the railway bridge at Iron Cove for three hours under water at a pressure of four atmospheres, had had only three minutes in the decompression chamber. On his way home he felt severe pain in his elbow; then he became semiconscious and was seriously ill for a week. His right knee swelled and developed a flexion deformity, which was corrected under general anæsthesia by Dr. A. Shewen. Abscesses developed behind the knee and in the region of the right trochanter. These were drained, and sinuses persisted for years. The patient went to England in 1883, but returned to Sydney unrelieved. Twynam examined him first in November, 1884, operated on the sinuses several times, and finally amputated the limb through the lower third of the thigh in October, 1885. The femur was completely necrosed, with an involucrum one-third of an inch thick surrounding it. The sinus persisted, and in January, 1886, Twynam removed the rest of the femur by Furneaux Jordan's method. The patient was restored to good health, but Dr. Alexander MacCormick had to excise a painful nerve while Twynam was on a visit to England.

The *Australasian Medical Gazette* in 1882 has an article by A. Shewen—and an editorial—on an outbreak of caisson disease at Iron Cove. Shewen's paper was presented at a meeting of the New South Wales Branch of the British Medical Association. Several members took part in the discussion, and a committee of six (including Twynam) was appointed to investigate the subject and report back to the Council of the British Medical Association. A few months later the editor (1883) mentioned that the Association had prevailed on the Government to grant compensation—albeit inadequate—to several men who had been paralysed.

The same volume of the *Australasian Medical Gazette* successively mentions the appointment of Twynam (recently arrived from London) as resident medical officer to Sydney Hospital, his resignation therefrom, his election to the British Medical Association, and his appointment as honorary assistant surgeon to the newly opened Prince Alfred Hospital. The "Australian Medical Directory" shows his address as Petersham in 1883, as both Petersham and 211 Macquarie Street in 1886, and as Darlinghurst in 1892.

Twynam's article of 1888 is well written and shows unusual solicitude for the patient and a knowledge of the literature. He recognized the condition as a rare sequel of caisson disease worthy of publication in the *British Medical Journal*, and he displayed considerable enterprise

in sending the paper to London. Moreover, reports in the *Australasian Medical Gazette* show that in 1887 he began a period of unusual activity. At British Medical Association meetings he took part in discussions on uræmia, strangulated hernia, tracheotomy, conjunctivitis and morphine poisoning. Then he read a paper on thyroidectomy, which was published in full (1887). He recommended subtotal thyroidectomy to relieve goitrous pressure on the trachea; he condemned the operation of simple incision of the isthmus.

During 1888 Twynam was at several meetings of the British Medical Association, and he read a paper advocating suprapubic cystotomy for vesical calculus, with a review of 67 cases from the literature (1888*b*). He was taken to task by Dr. Thomas Fiaschi for trying to revive a "discredited" operation. This paper was praised by Thane of Yass in 1889, and by Alexander MacCormick in the same year in an address to the Intercolonial Medical Congress in Melbourne. Twynam (1889*a*), who was now honorary surgeon to Prince Alfred Hospital, returned to the fray with another paper on vesical calculi.

Soon after this he presented a paper on five cases of acute intestinal obstruction due to different causes (1889*b*). During the discussion his exhaustive review of the subject and his elaborate specimens were praised. He mentioned acute appendicitis, which had been first described by Fitz three years before. Later Twynam (1891) addressed a meeting on acute appendicitis, but he was apparently too busy to publish the paper in full. In 1890 he was made an honorary member of the newly formed Western Medical Association. In May, 1892, he read a paper on three unsuccessful trephine cases. He had had, he said, too many successful cases to collect in the time at his disposal, so he restricted his remarks to those in which lessons could be learned from his mistakes. During 1893 and 1894 Twynam was present at several meetings, and in June, 1894, he proposed a vote of thanks to the Council at the annual meeting of the New South Wales Branch of the British Medical Association.

Return to London.

Earlier there had been signs that Twynam's gaze was becoming fixed on London. He presented a paper (1890*a*) to the Clinical Society of London (read by Rickman Godlee) on removal of a calculus from the lower end of the ureter. The report states that he was praised for his new idea (the anterior approach). He later reported a fatal case of traumatic subclavian aneurysm (1890*b*), and four cases of fractured patella treated with an encircling subcutaneous suture (1893). He claimed priority for himself in the technique. The operations were performed at Prince Alfred Hospital.

The "London Medical Directory" of 1900 shows Twynam's address as South Kensington (London) and lists the three above-mentioned papers, together with an address to the West London Medico-Chirurgical Society on nephrectomy during pregnancy (1898). In 1920 he was still at South Kensington and had written no more articles. In 1930 his address was Sevenoaks, Kent, and in 1940 he lived in Buckinghamshire. The *British Medical Journal* (Obituary, 1941) has the following obituary notice:

> The death on June 13 at his home in Buckinghamshire of Dr. George Edward Twynam at the age of 85 removes one of the few remaining links with the early pioneers of Listerian surgery. Educated at Univeristy College Hospital . . . he shared lodgings with three other students, one of whom was Victor Horsley. . . . After doing a house-appointment at his own hospital he obtained a post as house-surgeon in Sydney. When he arrived there he found the medical profession much interested in what they had heard and read of Lister's discoveries; but few of them had first-hand knowledge of the new antiseptic technique, and they welcomed a young surgeon who could show them how things were being done in London. The result was that Twynam soon found himself elected to the Honorary Staff of the Prince Alfred Hospital, Sydney, and later became lecturer on clinical surgery at the University. He was a successful general practitioner and consulting surgeon in Sydney for several years, but eventually returned home for private reasons. He then started in general practice in South Kensington, where he was well known for many years. . . . He retained his physical vigour in marked degree; when well turned 70 he was accustomed to take walks of 30 miles or even more, purely for recreation. He had many recollections of Sir Victor Horsley as a young man: one of Horsley's foibles which Twynam used to recount was his persistent refusal to pass his fellow students the mustard-pot at meals; he held that mustard was an artificial stimulant of the gastric mucosa, as harmful as alcohol. . . .

The "London Medical Directory" of 1900 lists one Alfred Ernest Edward Twynam of West Kensington, a graduate in 1892 of University College Hospital; he had not replied to the directory's *questionnaire*, and his name disappeared from later issues. Perhaps the "private reasons" for George's return to London are connected with this man, who must have been a relative.

Comment.

All Twynam's papers show originality, enterprise and a knowledge of the literature. They display an unusual reflectiveness which is prepared to admit and learn from one's mistakes. It is strange that he should have sacrificed his career as a leading Sydney surgeon in order to take up general practice in London. Apart from the family reasons, there is no doubt that London exerted a magnetic attraction on him and on many others in Sydney at this time. Edward Rennie (also a graduate of University College Hospital) resigned from Prince Alfred Hospital in 1898 and took his family to London; but he returned two years later (McDonald, 1952). Probably Twynam had visions of securing hospital appointments. But he had to take up a busy general practice and was able to write no more.

Summary.

George Edward Twynam, a London graduate who lived in Sydney from 1882 to 1894, reported in 1888 a case of decompression necrosis of bone. His writings for several years reveal him as a surgeon of unusual ability. But he returned to London and obscurity in general practice.

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ALCOHOL AND FATAL TRAFFIC ACCIDENTS.

By A. T. PEARSON,
Perth.

FROM the beginning of 1950 in the metropolitan area of Perth (population 369,000), it has been a routine procedure to take from all fatal traffic accident victims samples of blood and urine for estimation of alcohol content. The results of these tests are shown in Tables I and II.

I think it will come as an unpleasant and disturbing surprise to most people that, out of 218 tests performed, 92 (42·2%) revealed alcohol in the blood. If a blood alcohol content of 0·1% (100 milligrammes of ethyl alcohol per 100 millilitres of blood) is taken as the level of insobriety for the purposes of driving a motor vehicle—and this is the level accepted in other countries (for example, Denmark)—then 39·4% of these people killed were under the influence of alcohol. In simpler terms, four in every ten fatal traffic accident victims were dangerously under the influence of alcohol at the time of the accident. This is an appalling state of affairs, and indicates that much more attention must be fixed on eliminating the drunken driver.

It will be seen from the tables that 34·2% of motor-car drivers, 35·7% of motor cyclists and 45% of pedestrians had blood alcohol percentages of 0·1 and over. The figures for 0·2% and over are also shown.

Method of Collection of Blood Samples.

The sample of blood, five to ten cubic centimetres, is taken directly from the right auricle with a syringe thoroughly washed in fresh tap water, and placed in a glass-stoppered bottle. (These bottles are specially prepared by the Government Chemical Laboratories.) This is sealed and handed to the police constable attending the post-mortem examination, who takes the specimen to the Government Analyst. Urine is collected when possible. No blood or urine samples are taken from deceased persons if survival after the accident is greater than twelve hours, since most, if not all, of the alcohol is eliminated from the blood in this period.

It is extremely important that no antiseptic, methylated spirits or ether come in contact with the syringes or specimen bottles, otherwise the test is useless. It is advisable, when a routine such as ours is not possible, that the doctor collecting the specimen should himself wash the syringe and bottle and seal the latter.

Once the specimen is corked and sealed properly, the alcohol content will not vary for at least one week, and then it will diminish slightly, but never increase.

Since many of these blood tests have brought me into court to explain their significance, several interesting points regarding the analyses have arisen, and these have been incorporated into the analyst's technique to eliminate any possible chance of error in the analyses. Since this is a colorimetric test, one barrister asked whether we had colour-tested the analysts performing the test. We did, and found that one could not pass the Ishihara test; but on checking his with other analysts' results, we could find no errors. However, it would be advisable for laboratories to employ on this work only analysts with normal colour vision. Other points which arose were the preparation of the reagents by each analyst himself, the periodic preparation of new reagents and the performance of blank estimations.

Determination of Alcohol in Blood.

The method used at the Government Chemical Laboratories, Perth, for the determination of the blood alcohol content is based on that described by J. S. Stevens and C. J. Gentzkow (1946), and modified by B. L. Southern. Some features of the Kozelka and Hine method (1941) have been incorporated.

Three thick-walled "Pyrex" boiling tubes, approximately 18 centimetres long and of three centimetres' bore, are connected in series by glass tubing passing through close-fitting rubber stoppers, so that air may be drawn successively through the solutions in each. To the first tube are added four millilitres of sample, together with ten millilitres of 10% sodium tungstate solution and ten millilitres of N/1 sulphuric acid; to the second are added four millilitres of Scot-Wilson reagent[1] and six millilitres of distilled water; and to the third are added nine millilitres of Anstie's reagent, modified, stronger.[2] Plugs of loosely packed glass wool are used to break frothing in the first and second tubes.

The apparatus is placed in a boiling water bath, and aeration by means of controlled suction is continued for thirty minutes, when distillation of alcohol is complete. When necessary, the volume of the solution in the third tube is reduced to nine or ten millilitres by further aeration in hot water. The solution is then cooled, transferred to a tube uniform with those containing the standards, and made up to a volume of ten millilitres with distilled water.

The colour developed in the dichromate solution is compared with a series of standards graduated in suitable steps, so that the percentage of alcohol within the range 0 to 0·35% weight for volume may be read directly. The standards are prepared by adding to nine millilitres of Anstie's reagent the calculated volume of 2% weight for volume alcohol solution, making the mixture up to ten millilitres with distilled water, and heating it for several minutes in boiling water.

[1] Scott Wilson reagent. Dissolve 90 grammes of sodium hydroxide in 300 millilitres of water. When cool, add this to a solution of five grammes of mercuric cyanide in 300 millilitres of water. Mix thoroughly, then add with constant stirring a solution of 1·45 grammes of silver nitrate in 200 millilitres of water. Any precipitate formed should be filtered. On account of its poisonous nature, this solution is measured by cylinder.

[2] Anstie's reagent, modified, stronger. Dissolve 7·4 grammes of pure potassium dichromate in 300 millilitres of distilled water. Add slowly, with constant stirring, 560 millilitres of pure concentrated sulphuric acid. Dilute to 1000 millilitres with distilled water.

TABLE I.

Fatal Traffic Accidents in Western Australia, 1950 to 1956 Inclusive.

Victims.	Fatalities.	Males.	Females.	Blood Alcohol Test Not Performed.	No Alcohol Found.	Blood Alcohol Content Less than 0·1%.	Blood Alcohol Content Between 0·1% and 0·2%.	Blood Alcohol Content More than 0·2%.
Motor vehicle drivers ..	64	60	4	13	29	2	8	12
Motor vehicle passengers	67	41	26	67	—	—	—	—
Motor cycle riders ..	104	104	0	34	45	0	14	11
Pillion passengers ..	15	12	3	8	2	0	5	0
Push cycle riders ..	30	27	3	20	8	1	1	0
Pedestrians	194	132	62	114	42	3	5	30
Totals	474	376	98	256	126	6	33	53

Interpretation of Results.

It has been shown that Australian beer contains about 4·5% of ethyl alcohol by volume. Taylor (1954) considers that ten ounces (half a pint) of beer will give a blood alcohol concentration of 0·016% after two hours, twenty ounces will give 0·032%, and so on. This is for an average man. For a very large man, more would be required to produce the above-mentioned percentages. It is also well established that the human body eliminates alcohol at a rate of 0·02% per hour. After alcohol has been taken into the stomach, it is quickly absorbed into the blood and

TABLE II.

Blood Alcohol Test.	All Fatal Road Accidents.	Motor Vehicle Drivers.	Motor Cycle Riders.	Pedestrians.
Blood alcohol test performed.	218	51	70	80
Positive result to blood alcohol test.	92 (42·2%)	22 (43·1%)	25 (35·7%)	38 (47·5%)
Blood alcohol content of more than 0·1%.	39·4%	39·2%	35·7%	43·7%
Blood alcohol content of more than 0·2%.	24·3%	25·5%	15·7%	37·5%

thence into most tissues, very little being taken up by bone or fat. Oxidation in the body removes most of the alcohol. What is left is eliminated chiefly by the urine, small amounts being eliminated by the breath and skin. The urine alcohol content is higher than the blood alcohol content in the proportion 5:4, once absorption and elimination have been stabilized.

It can be taken that with up to 0·05% of alcohol in the blood there is little impairment of ability to drive a motor vehicle; between 0·05% and 0·1% impairment commences; from 0·1% upwards, most drivers are no longer safe. After all, this represents a minimum of three pints of beer or six full whiskies—a considerable amount of alcohol. At 0·15% and above, there are practically no safe and capable drivers. Although minimum quantities of alcohol are quoted here and elsewhere, we are concerned, not with the amount of alcohol which a person drinks, but with the actual percentage which is in his blood, and which has been well proven to indicate the state of sobriety.

Reception of the Test by Law Court.

When the interpretation of the results of the blood alcohol estimations were first given in the Coroner's Court, there was marked opposition by the legal profession, and many hours were spent in lengthy explanations and debate. By means of lectures to the Law Society, personal explanations, articles in the *West Australian* and legal battles, I think I can safely say that the blood alcohol test is accepted equally by the Supreme Court, the Police Court and the Coroner's Courts, and has put the determination of alcohol intoxication on a scientific bases. In a recent case in the Supreme Court, the judge expressed the opinion that he regarded the blood alcohol test as being like any other accepted chemical test, and, therefore, acceptable in the court. Insurance claims arising out of motor accidents in which drunken drivers are concerned, as proven by the blood alcohol test, are now frequently rejected.

Many motor drivers charged with being under the influence of alcohol now ask for a blood test; but this is not always made, since doctors are not keen to attend the police station to take the blood sample, and there are few facilities available at a police station to assist the doctor in this work. Once these difficulties have been overcome, many more charged drivers will volunteer for the test. It is of interest to know that quite a few suspected drunken drivers have been acquitted on the results of the blood test.

Conclusion.

This work was started, first, to gain experience as to the part played by alcohol in road fatalities, and secondly, to introduce the blood alcohol test to the courts. The figures are illustrative and alarming. The test is firmly established in the courts in this State, and now the next step must be the introduction of compulsory or, failing this, voluntary blood tests for motor drivers suspected of being under the influence of alcohol.

Summary.

1. The results of 92 blood alcohol tests carried out on fatal traffic accident victims are presented.

2. The method of calculation and the precautions to be taken are outlined.

3. The reception of this test in the Western Australian law courts is mentioned.

4. The hope is expressed that the blood alcohol test will become the standard test for the determination of the drunken driver.

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Reviews.

Annual Review of Medicine. Edited by David A. Rytand and William Creger; Volume VIII; 1957. Palo Alto, California: Annual Reviews, Incorporated. 8¾" × 6", pp. 540. Price: $7.50.

As previously, David A. Rytand is the editor of this book, and William Creger is the associate editor. There are 23 papers, each contributed by invitation by one or more authors, referred to by the editors as "authorities in their respective fields". Lack of space has made it necessary to omit the annotated list of reviews in medicine which has usually been included. The book covers a comprehensive list of subjects, and will be helpful to specialist physicians and also to general practitioners with a physician bias.

Lumbar Puncture and Spinal Analgesia. By Sir Robert Macintosh, M.A., D.M., F.R.C.S. (Edin.), F.F.A.R.C.S., M.D. (hon. causa), Buenos Aires and Aix-Marseilles, Hon. F.F.A.R.A.C.S.; Second Edition; 1957. Edinburgh and London: E. and S. Livingstone, Limited. 8¾" × 5¾", pp. 152, with 111 illustrations. Price: 25s.

THIS is a very interesting, though somewhat unusual, book. It rather belies its title, for the author goes far beyond the limits encompassed by lumbar puncture and spinal anæsthesia, which takes up less than half the book. This, however, does not detract from its value.

The author first deals with the history of lumbar puncture, and then he discusses in great detail the anatomy of the spinal column and its contents. He allocates a chapter to the cerebro-spinal fluid, and deals with its formation, its circulation and its absorption, together with its composition, functions and volume *et cetera*. Other chapters are devoted to sterilization, to the technique of lumbar puncture and to the administration of spinal anæsthesia.

The only point on which we disagree with the author is in regard to his treatment of headache following lumbar puncture. It is unnecessary to inject fluid into the subarachnoid space, and such a procedure is extremely dangerous because of the risk of infection. The insertion of a catheter into the spinal theca and leaving it there are

also contraindicated for the same reason, and also for another reason; it would merely serve to make another hole in the dura and arachnoid and keep it open. When the catheter was removed, the original state of affairs would still exist, although the primary opening might even have sealed over. The treatment of headache following lumbar puncture is simple, effective and completely devoid of risk. It merely consists of elevating the foot of the bed on twelve-inch blocks and forcing the intake of fluids to six to eight pints or more per day. This is preferably done with the patient in the prone position, without a pillow, for as long as can be tolerated. The headache invariably disappears within a few days.

The book is literally filled with really excellent illustrations—drawings, diagrams and photographs. It will be of considerable value to the anæsthetist, and also to the neurosurgeon and the orthopædic surgeon.

1957 Medical Progress: A Review of Medical Advances during 1956. Edited by Morris Fishbein, M.D.; 1957. New York, Toronto, London: McGraw-Hill Book Company, Incorporated. 9" x 6", pp. 382. Price: $6.00.

This book, edited as usual by Morris Fishbein, contains articles by 29 authors on the following subjects: medicine, cardio-vascular disease, neurology, endocrinology, gastroenterology, general surgery, obstetrics, allergy, psychiatry, diabetes, rheumatic diseases, nutrition, dermatology, ophthalmology, physical medicine and rehabilitation, oto-laryngology, new drugs, orthopædics, laboratory procedures. Each aims to present a review of the most important advances in the subject made during 1956. Naturally, it would be impossible within the compass of one volume to do this in any detail; but the brief résumés given are sufficient to call attention to profitable avenues of further reading, and the extensive bibliography at the end of each section makes the search relatively easy. This book has a real, though rather limited, sphere of usefulness.

A Synopsis of Children's Diseases. By John Rendle-Short, M.A., M.B. (Cantab.), M.R.C.P., D.C.H.; Second Edition; 1957. Bristol: John Wright and Sons, Limited. 7¼" x 5", pp. 636.

The popularity of this synoptiform volume is proved by the appearance of a second edition, three years after the first. Certainly the 624 pages contain a great amount of tabulated details, and if they had been fully expanded into linear form a huge volume would result. There are only a very few sketchy illustrations, and so no space is taken from the written work. Students can conjure up pictures of actual patients as mental illustrations for the text.

The author at all times has a very practical clinical approach to the topics discussed, and the benefits of his own experiences are obviously being passed on; throughout he explains the salient points in both diagnosis and therapy.

The form of the work enables students to make a quick revision of the subject; but it also will help busy practitioners to avail themselves of its aid without having to delve too far into the background when a quick reference for an emergency is needed. Dr. John Rendle-Short is to be congratulated on his excellent synopsis of this important branch of medicine.

Peripheral Vascular Disorders. Edited by Peter Martin, V.R.D., M.Chir., F.R.C.S.Ed., R. Beverley Lynn, M.D., F.R.C.S., J. Henry Dible, M.B., LL.D., F.R.C.P., and Ian Aird, Ch.M., F.R.C.S.; 1956. Edinburgh and London: E. and S. Livingstone, Limited. 10" x 7", pp. 855, with many illustrations. Price: £5 10s.

There are nine distinguished contributors to this excellent volume on peripheral vascular disorders, which covers minutely the many and varied conditions caused by arterial diseases and reactions to environments. The presentation is complete, in that it is introduced with descriptions and discussions of the anatomy and physiology of the autonomic nervous system, the anatomy of the peripheral vessels and the consideration of collateral supplies. Chapters follow devoted to cardinal signs, together with methods of examination and the special means of investigation. An interesting account of plethysmography is included here. A most useful survey of the radiological changes accompanying peripheral vascular disease follows, divided into two sections—the significant appearances in plan X-ray films, and those shown by arteriography. The authors then proceed to descriptions of the various conditions with which the clinician comes in contact either commonly or uncommonly. The numerous diseases are discussed clearly and fully, and when there is any contentious factor in ætiology, the several points of view are presented with pertinent comment. Chapters are also included on arterial injuries and emboli, responses to environment and vasospastic states, together with their diagnosis and treatment; nor are venous, arterio-venous and lymphatic conditions overlooked.

The book is lavishly illustrated in both colour and black and white, the reproductions being of high quality. These illustrations combine with the lucidly written text to provide an unusually good book of reference upon an interesting subject, the scope of which has widened enormously in recent years.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"International Congress of Gastroenterology: Fifth Meeting of L'Association des Sociétés Européennes et Méditerranéennes de Gastro-Entérologie: London, July 18-21, 1956." Basel and New York: S. Karger. 9¾" x 6¾", pp. 655, with illustrations.

The papers read at the congress are published in full or in condensed form with some of the discussions.

"Recent Outbreaks of Infectious Diseases", by S. Leff, M.D., D.P.H.; 1957. London: H. K. Lewis and Company, Limited. 8½" x 5½", pp. 420. Price: £1 15s.

Describes and discusses outbreaks of infectious disease that have occurred in England and Wales in recent years.

"Orthopedic Surgery in Infancy and Childhood", by Albert Barnett Ferguson, jnr., B.A., M.D.; 1957. Baltimore: The Williams and Wilkins Company. Sydney: Angus and Robertson, Limited. 10" x 7", pp. 520, with 504 illustrations. Price: £8 5s.

Covers the whole related field except fractures.

"Plaster of Paris Technique", by Marian English, S.R.N., R.F.N.; 1957. Edinburgh and London: E. and S. Livingstone, Limited. 8½" x 5½", pp. 136, with 133 illustrations. Price: 15s.

Written primarily for nurses working in a hospital fracture department.

"Medical Research Council Memorandum 34: The Treatment of Wound Shock: The Wound Shock Working Party"; 1957. London: Her Majesty's Stationery Office. 9¾" x 6", pp. 48, with four illustrations. Price: 3s. 6d.

A new edition (rewritten) of War Memorandum No. 1.

"Blood and Bone Marrow Patterns", by G. D. Talbott, M.D., Elmer R. Hunsicker, B.S., and Jonah Li, M.D.; 1957. New York and London: Grune and Stratton. 12" x 9", pp. 60, with many illustrations. Price: $12.00.

The authors have aimed to present, by means of coloured photomicrographs, blood cell patterns as seen from bone marrow aspirations in various abnormal conditions.

"Ciba Foundation Colloquia on Ageing: Volume 3: Methodology of the Study of Ageing", edited by G. E. W. Wolstenholme, O.B.E., M.A., M.B., B.Ch., and Cecilia M. O'Connor, B.Sc.; 1957. London: J. and A. Churchill, Limited. 8" x 5¼", pp 214, with 47 illustrations. Price: 32s. 6d.

The title is self-explanatory. Twelve papers are presented with accompanying discussion.

"Pulmonary Complications of Abdominal Surgery", by Anthony R. Anscombe, M.S. (Lond.), F.R.C.S. (Eng.); 1957. London: Lloyd-Luke (Medical Books), Limited. 8½" x 5½", pp. 132, with 36 illustrations. Price: 20s.

An account of experimental and clinical experience.

"The Essentials of Materia Medica, Pharmacology and Therapeutics", by R. H. Micks, M.D. (Dublin), F.R.C.P.I.; Seventh Edition; 1957. 8" x 5¼", pp. 442. Price: 28s.

The book has been revised and partly rewritten since the previous edition was published in 1954.

"The Doctor, His Patient and the Illness", by Michael Balint, M.D.; 1957. London: Pitman Medical Publishing Company, Limited. 8½" x 5½", pp. 368. Price: 60s.

The result of an investigation by fourteen general practitioners and a psychiatrist.

The Medical Journal of Australia

SATURDAY, AUGUST 3, 1957.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of the article. The abbreviations used for the titles of journals are those adopted by the Quarterly Cumulative Index Medicus. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

ANTIBIOTICS GALORE.

Several hundred tons of antibiotics are used each year in the United States. The figure for Australia is not known to us, but there seems little reason to doubt that proportionately it would not lag far behind the American figure. However, the most notable feature about antibiotics consumed today is not their total quantity but their variety—their name is legion. The average clinician must find it difficult in the extreme to keep up with them in such a way as to give his patients the maximum advantage of current developments. Those who find it impossible to cope with the voluminous literature on the subject will welcome the eminently practical worksheet prepared by the Antibiotics Committee of the National Health and Medical Research Council and published in this issue under the general heading of "Medical Practice". Read in conjunction with its accompanying notes, the table of antibiotics will tell the clinician most of what he wants to know and should retain its current value for some time. It is recommended that it be kept handy for reference. Its routine use should help to overcome the misuse of antibiotics, on which there has been so much unhappy but necessary comment.

One subject to which a good deal of attention has been paid recently in various overseas medical journals is the use of antibiotics in combination. It is also the subject of over a dozen papers in the latest "Antibiotics Annual". As this approach to antibiotic therapy receives only passing comment in the Antibiotics Committee's worksheet, something more may with advantage be said here. In his introductory remarks in the "Antibiotics Annual"[1] Henry Welch states that it is quite possible that we are now in a third era of antibiotic therapy, the first being the era of the narrow-spectrum antibiotics (penicillin and streptomycin), the second the era of broad-spectrum therapy, and the third an era of combined therapy in which combinations of chemotherapeutic agents, particularly synergistic ones, will be customarily used. Of the papers in the "Antibiotics Annual" which deal with these combinations, the first group describe experiences in the use of combinations of oleandomycin with oxytetracycline and with tetracycline in the management of a wide variety of infections. The points mainly looked for are control of the infection, minimization of side effects and avoidance of or delay in the emergence of resistant strains of organisms. The conclusions are in general favourable. The other group of papers are concerned with the effect on the intestinal flora of various combinations of antibiotics and other antibacterial agents. The object is to overcome the upsetting of the normal balance of the intestinal flora and the overgrowth of undesirable organisms, and at the same time to promote adequate intestinal antisepsis. The evidence presented suggests that there is merit in certain of these combinations, but experience is still too limited for clear conclusions to be drawn. The matter will bear further investigation, particularly in view of the fact that the use of combinations of antibiotics, other than in a small group of specific instances, has been viewed critically in a number of quarters. The pros and cons are presented in a report by Harry F. Dowling,[2] the publication of which has been authorized by the Council on Pharmacy and Chemistry of the American Medical Association. Dowling agrees that in a few highly selected conditions the administration of combinations of antibiotics is justified; in some other cases, it may be not only useless but actually harmful. His recommendation is that when combined therapy of antibiotics is indicated, the antibiotics are best given separately, except in the case of mixtures for local application to the skin. Another reference which we may mention occurs in a paper on the erythromycin group of antibiotics by Lawrence P. Garrod,[3] Professor of Bacteriology in the University of London. He refers to the original paper by A. R. English, T. J. McBride, G. Van Halsema and M. Carlozzi[4] on their study of a tetracycline-oleandomycin combination in a 2:1 mixture. They reported that the combination had synergistic activity *in vitro* against selected microorganisms, marked ability to retard the emergence of antibiotic-resistant variants of certain strains of *Staphylococcus pyogenes* and *Streptococcus pyogenes*, and statistically significant synergistic activity *in vivo* against infections in mice with both normal and antibiotic-resistant strains of the same organisms. Garrod was unable to reproduce all the findings of English and

[1] "Antibiotics Annual, 1956-1957: Proceedings of the Fourth Annual Symposium on Antibiotics", edited by Henry Welch, Ph.D., and Félix Martí-Ibáñez, M.D.; 1957. New York: Medical Encyclopedia, Inc. 10" × 6¾", pp. 1152, with many figures. Price: $10.00.

[2] *J.A.M.A.*, 1957, 164:44 (May 4).

[3] *Brit. M. J.*, 1957, 2:57 (July 13).

[4] *Antibiotics & Chemother.*, 1956, 6:511 (August).

his colleagues. His experiments failed to demonstrate the synergistic action claimed for the tetracycline-oleandomycin combination. In a study of habituation, six strains of *Staph. pyogenes* were habituated to each antibiotic and to the combination. The increased resistance obtained to each single antibiotic, which was somewhat larger to oleandomycin, was unaccompanied by a change in sensitivity to the other, or by much change in sensitivity to the combination, since the second retained its activity. In habituation to the combination, the tetracycline component seemed to play the dominant part, and resistance to it increased almost as much as to tetracycline alone; sensitivity to oleandomycin changed comparatively little, and sensitivity to the combination changed to an intermediate degree. Garrod comments that it seems that the smaller amount of the weaker antibiotic fails to interfere effectively in the reaction of the organism to the major component in the combination.

It will thus be seen that two widely divergent views on the use of antibiotics in combination are currently held by investigators in this field. No doubt further laboratory and clinical experience critically considered will reveal the truth of the matter. Meantime, nothing has occurred to lessen the importance of an informed and conservative use of antibiotics at all times if they are to perform their reasonable therapeutic service.

THE NEED FOR DOCTORS IN INDONESIA.

Not the least of the problems of the young Republic of Indonesia is the difficulty being experienced in the provision of medical care for the Indonesian people. In a total population of approximately 80,000,000 people there are only about 1500 doctors; this gives a proportion of approximately one doctor for every 55,000 people, as compared with the Australian figure of approximately one doctor for every 1000 people. A high proportion of the doctors are concentrated in the cities, so that in some of the areas away from the cities there is only one doctor for 250,000 people. When to this tragic shortage of medical practitioners we add the difficulties of communication and transport and the relatively primitive conditions in many areas, the problem is seen to be very great indeed. For this reason the Government of Indonesia is anxious to obtain the services of foreign doctors on a special short-term contract. Details of this arrangement are set out elsewhere in this issue under the heading "Medical Practice".

During a recent visit to Australia, the Secretary-General of the Indonesian Ministry for Health made a strong plea for Australian doctors to go to Indonesia for periods of three years on short-term contract. He made it clear that, while the remuneration offered is not lavish by Australian standards, it is possible to supplement this from private practice, permission to carry on which can be obtained after a short initial period. Australian doctors already in Indonesia appear to have made a favourable impression and smoothed the way for any of their colleagues who are interested to take up this challenge. While appealing for help in this way, the Indonesian authorities do not understate the practical difficulties in their working conditions that foreign doctors in Indonesia may have to face. It is pointed out that they have to deal with a situation quite different from that with which they are familiar in European and similar countries. The main task is that of providing general medical care, but a prominent place is occupied by the treatment of tropical diseases, such as malaria, frambœsia and ancylostomiasis. Medical care has to be given mainly in rural districts, where hospitals are few and modern means of diagnosis and treatment are often not available. This does not mean that there are no big hospitals in the towns, but there are not many vacancies on the staffs of these hospitals. It is also made clear that, as a rule, no definite promise can be made with regard to the place to which a foreign doctor will be sent. When he arrives in the country he is sent to the place where his help is most needed; however, personal interests are certainly taken into consideration. The housing shortage is particularly acute in Indonesia, and it may be difficult to find accommodation in the towns other than in a mess or an hotel. In country areas the difficulty is often overcome by the fact that the local authorities, anxious to have a doctor, make it their business to find suitable accommodation for him.

Not unnaturally, the Indonesian Government would like to have Indonesian doctors caring for their own people, but the numbers at present available and the facilities for the training of medical students are so limited that it is unlikely that the country can provide for its own needs for a good many years to come. The Australian doctor undertaking this work needs to be something of an idealist, but idealism is worth cultivating in the modern world, and this particular need is one with which Australian doctors may well concern themselves. Indonesia is our nearest neighbour and, as a young nation born into a troubled world, must have practical help from other countries if its development is to be sound and healthy. Quite apart from idealistic considerations, the welfare of Indonesia is of hard, practical importance to Australia. Indonesia has great natural resources and the capacity to develop into a self-supporting, happy nation, with fewer problems in this direction than many other Asian countries. Economic and social stability in this neighbour country is of great importance to Australia. Young Australian doctors with a little enterprise and vision can make a major contribution to this need. Inquiries should be directed to the Indonesian Embassy in Canberra.

Current Comment.

PULMONARY COMPLICATIONS OF ABDOMINAL SURGERY.

A specialist with the enterprise to borrow a technique or an idea from another specialty and apply it or adapt it to his own very often produces results which are of great interest and importance. This statement is directly applicable to the work of A. R. Anscombe,[1] a surgeon who borrowed a modern spirometer and fast-moving kymograph and took them into the surgical wards at the London Hospital. Anscombe's enterprise is almost as exciting as it is to find a spirometer in the right place, which is in the

[1] "Pulmonary Complications of Abdominal Surgery", by Anthony R. Anscombe, M.S. (Lond.), F.R.C.S. (Eng.); 1957. London: Lloyd-Luke (Medical Books), Limited. 8¼" × 5½", pp. 132, with 36 illustrations. Price: 20s.

ward rather than the laboratory. The results of this work form the most important part of a monograph on the pulmonary complications of abdominal operations. The spirometric tracings taken from patients before and after a variety of abdominal operations were those of a maximum forced expiration and inspiration. From these, figures for the vital capacity, maximum expiratory rate and maximum inspiratory rate were obtained, and it is upon percentage changes in these values that the conclusions described below are based. The physiological basis and interpretation of these tests need not be discussed here. Suffice it to say that they are related to the patient's mechanical ability to ventilate, and they are easily performed even by moderately ill patients. In the present summary, the general term "ventilatory capacity" is used to refer to all three measurements, the changes in which ran parallel; the figures given are therefore approximate, and they relate to the first post-operative day. Operations performed through a right upper paramedian incision or an upper mid-line incision led to a fall of about 65% to 70% in ventilatory capacity. The loss was similar whether the operation was an extensive one, such as partial gastrectomy, or a relatively brief exploratory laparotomy; cholecystectomy (Kocher's incision was not used) was exceptional in producing a fall of only 50%. Anscombe stresses his finding of only a 50% loss after transthoracic gastrectomy in two patients, as compared with 65% in patients who had partial gastrectomy and other operations performed through incisions involving more of the upper abdominal wall. He suggests that the former approach might well be preferred. This is a dangerous conclusion; the statistical significance of these results may well be questioned, particularly in view of the 50% loss for cholecystectomy through the same abdominal incision. Lower abdominal operations of various types led to a loss of 25% to 40% in ventilatory capacity, but no significant change was noted after minor gynæcological procedures or operations upon limbs. The results after operations on the kidneys were particularly revealing: whereas Mayo's incision was associated with a 20% reduction in ventilatory capacity, a transverse incision led to a fall of 55%. Anscombe advises that the latter incision should be reserved for cases in which the extra exposure is essential. Broadly speaking, ventilatory capacity after these procedures remained abnormal for about a week, progressive improvement beginning on the second day.

Pulmonary complications after abdominal surgery tend to be more frequent after operations for acute inflammatory lesions, and Anscombe implies that this may be related to the low values for ventilatory capacity tests obtained pre-operatively in, for example, acute appendicitis and perforated peptic ulcer. Anscombe's figures indicate a pre-operative fall of 75% in three patients with perforated ulcers: all the vital capacities were below a litre. A person with healthy lungs copes with this threat to the maintenance of normal alveolar ventilation by increasing his respiratory rate to between 20 and 30 breaths per minute; the situation for a patient with even slight emphysema, in whom the respiratory dead space is increased and who may have difficulty in reaching even a rate of 20 per minute, may well be desperate. Anscombe believes that hypoventilation may be an important factor in unexplained deaths of older patients with peritonitis, as well as of those whose lungs are hypoventilated after operations.

Anscombe investigated several factors which might influence ventilatory capacity other than the operations and the incisions used. His observations suggest that morphine improves ventilatory capacity in the early post-operative period, and that abdominal binders, on the other hand, are probably not much help. The most significant of his studies on the influence of posture emphasizes the undesirability of using a steep Trendelenburg tilt for any length of time: he produces experimental evidence to indicate that pneumatic cuffs applied to the legs and inflated to a pressure of 60 millimetres of mercury are likely to reduce the risks involved.

By no means all of this useful little book is devoted to physiological studies, although these form the most interesting and original sections of the work. Most of the factors related to the development of pulmonary complications generally are considered; to a sound review of the literature the author adds observations based on his thorough study of 146 patients undergoing abdominal operations. The clinical aspects of post-operative pulmonary infections, embolism and collapse are satisfactorily described. A number of highly debatable statements and several loose ones are to be found, particularly in the sections dealing with ætiological and physiological factors in the development of some of these complications. No useful purpose would be served by enumerating these, but it may be worth stressing that the tests of ventilatory capacity employed in this investigation are a piece of respiratory gymnastics which the post-operative patient, or any other person, is never called upon to perform in real life. They demonstrate the presence of abnormality, but what the significance of this abnormality is in the resting state is a matter for further experiment. Of course, when the values obtained are critical, as in the subjects with perforated ulcer, the results are more directly applicable to the patient's clinical state.

Two criticisms may be mentioned which may occur to clinical research workers, but which may be deemed academic by the clinician. The first is that the graphical presentation of the results, which is otherwise very satisfactory, might well have included the range or standard deviation as well as the mean for percentage change. The second is the total absence of reference to absolute values, which would have provided valuable data for other workers and for those interested in obtaining answers to other questions. Does, for example, the ventilatory capacity fall more in those whose pre-operative values suggest emphysema than in those whose initial results are normal?

Finally, the clinician may be reassured that the diagrams and digression concerning the exponential form of the expiratory curve, near the beginning of the book, are largely irrelevant, and the remainder of the book is eminently readable. Whether Anscombe will convince the surgeon that pre-operative ventilatory capacity studies are "as essential as the knowledge of the hæmoglobin and the blood group" remains to be seen, but he has done a great service in directing attention to their relevance, and to their practical application.

RECURRENT APHTHOUS ULCERATION OF THE MOUTH.

RECURRENT aphthous ulceration of the mouth was first clearly described in 1888 by Jvon Mikulicz and W. Kümmell, and the first description in English was given by Sibley in 1899. During the past fifty years numerous papers have appeared, mostly describing a few cases, and the lack of understanding of the condition is indicated by the existence of twelve synonyms for the disorder. The condition is relatively common and can be very disturbing to the patient; it certainly deserves more than the few lines given to it in most text-books of medicine and diseases of the skin. W. Sircus, R. Church and J. Kelleher[1] have reviewed the literature on the disorder and have given a thorough account of the frequency, symptoms and treatment observed by themselves. They state that the buccal lesions are frequently associated with similar ulceration elsewhere, and lesions on the genitals, eyes and skin have been noted with or without buccal lesions.

In order to determine the frequency of the condition 1000 patients consecutively attending out-patient clinics of the Royal Infirmary, Sheffield, were questioned, and those who admitted to having had the disorder were referred to Sircus and his colleagues. At the same time 587 patients at the Western General Hospital in Edinburgh were questioned, as well as 151 patients in a private practice. The overall incidence for all ages and both sexes in the

[1] *Quart. J. Med.*, April, 1957.

1738 patients questioned was 335 (19·3%); so the condition is a common one. One hundred and twenty patients with ulceration were studied in detail. The highest incidence of onset in both sexes was in the second decade. In 10% of the female patients the first attack occurred between the ages of fifty and fifty-nine years. There appeared to be a rhythmical periodicity in the attacks in most subjects, but at shorter intervals in the female. In some of the patients the disorder had recurred over a period of more than forty years. A study of factors precipitating attacks showed that mental stress of some form preceded the attacks, and local trauma often played a part. The commonest sites of the ulcers were inside the cheeks opposite the upper molars and inside the lips. Involvement of vulva or vagina often occurred.

A remarkable diversity of treatment is seen in published accounts of the disease, but none of them seem to have been very effective. In this series folic acid, nicotinic acid, riboflavin, vitamin *B* complex, ethisterone, cortisone, locally administered "Aureomycin" and radiotherapy were tried in the best approved methods for testing drug activity. No significant change in the progress of the disease was seen, except with radiotherapy, from which one patient had a complete remission for three months, and another obtained partial remission from local application of a suspension of "Aureomycin". In the latter case there was no change in the number or frequency of the ulcers, but considerable analgesic effect in all cases. A thorough investigation was made as to the relation of the condition to *herpes simplex* and to a virus ætiology. It was established that there was no relation to *herpes simplex*. No virus was grown on chick egg membrane.

That the condition is very much more common than is usually believed has been established. The fact that thorough study has failed to provide any evidence regarding ætiology, and the almost complete failure of all modes of treatment tried, with the exception of the relief afforded by "Aureomycin", are to be deplored. The condition is one which could form a useful study for a practising medical man. It is interesting that two of the three authors of the paper were susceptible to the disorder. There is a good coloured plate attached to the paper showing lesions on the cheeks, lips, tongue and vagina.

THE RESPONSE OF MALIGNANT TUMOURS TO RADIATION.

RADIATION from radium or other radioactive element or from an X-ray tube has been used for many years for the treatment of malignant tumours and seems to be the only known agent which has any destructive action on malignant tumour cells. How and why the radiation kills the malignant cells rather than the normal cells is not known. C. A. Pannett[1] has put forward an interesting suggestion to explain this action. He points out that much work has been done on the placing of radium needles in relation to a tumour, and it seems now to be widely believed that the best results are obtained when the radium needles are put in the healthy tissue surrounding the growth. If the tumour is at the centre of a sphere of radiating needles, it gets more radiation than the zone in which the needles lie. It is agreed that the less radiation the normal tissue gets the better. Why then are the needles not placed in the tumour itself, which should receive the maximum amount of radiation if the present belief is true? It is possible that the radiation does not work by affecting the malignant cells directly. Pannett suggests that, on present evidence, it is quite as sensible to believe that the radiation, acting on normal cells, alters their metabolism, so that they produce substances which are antagonistic to the agent which causes cancer or to the cells which have been altered, and that these substances, being carried by the lymph-stream to the area of growth, cause death of the cancer cells. What evidence is there for such a view? There is, as yet, no direct evidence, but there is, so Pannett believes, some strong indirect evidence. Early work on the use of radium needles in the treatment of mammary cancer showed that the best results were obtained by implanting radium needles in the healthy breast tissue all around the tumour. To ensure a correct diagnosis a small piece of the tumour was removed for histological examination. While the primary tumour disappeared in many cases, carcinoma was apt to grow afterwards in the skin scar resulting from the biopsy. The cells of the growth in their original position died, while the carcinoma cells transplanted to the skin grew. Any substance produced by the irradiation of normal cells would pass by the lymphatics to the tumour tissue. The lymphatics of the true breast tissue form a plexus around the alveoli, and there is no direct communication between these and the skin and subcutaneous lymphatics. Thus any substance produced by the irradiation of the normal alveolar cells would pass to the tumour cells *in situ*, but not to the transplanted cells in the subcutaneous tissue and skin. That the hypothetical substance does not affect metastases could be accounted for by the considerable dilution of the substance at a distance from the radiation. There is no proof that any such substance is produced, nor have we any idea how radiation affects cells, normal or malignant, but the idea is suggestive and seems well worth investigating.

[1] *Lancet*, April 20, 1957.

GLUCAGON: ITS PRESENT POSITION.

THE second hormone of the pancreas, glucagon, has now arrived, and H. Elrick, A. Staub and H. Maske,[1] who have contributed to its isolation and the understanding of its working, present the reasons for its accepted status. In recent work Bromer and others have accomplished its complete structural analysis, and its straight chain molecule of 29 amino acids has provided final evidence that insulin and glucagon are two different entities, dissimilar in amino-acid content and structure. Traces of zinc are often found with glucagon and can readily be made to combine with it. Because of this it was originally considered that the combination was a prerequisite for biological activity, but it has been found that crystalline glucagon-zinc and glucagon alone do not differ biologically. The physiological significance of the binding, if any, is still not clear.

The source of the hormone is the alpha cell, and Bencosme and others have done much to resolve the apparent discrepancies in the evidence of its origin by making use of the regional differences in alpha and beta cells of the pancreatic islets of the dog. In the dog the uncinate process is devoid of alpha cells, and extracts of this area of the pancreas from normal and alloxan-diabetic animals were found to be virtually lacking in any hyperglycæmic activity. Many of the discrepancies have been based on the assumed specificity of cobalt chloride for depressing glucagon production by damage to the alpha cells. Bencosme and his colleagues point to the discrepancies in experimental procedures, regional differences in alpha-cell content, species difference in response to cobalt and differences in morphological findings in such reports. They were unable to produce any visible change in alpha cells of the rabbit, rat, dog or chicken, and Fodden has confirmed this in the monkey, dog, cat, rabbit, rat and teleost fish. Despite many attempts with substances other than cobalt chloride, no drug has been found having a direct and permanently destructive action on the alpha cells comparable to the effect of alloxan on the beta cells.

There is no evidence at present to support a direct functional relationship between the anterior pituitary lobe and the alpha cells. In the adult rat no appreciable change occurs in blood sugar level or in morphology of the islets for periods up to four or five months after hypophysectomy, and growth hormone has a dubious effect on the morphology of the islets after three weeks, no change occurring in carbohydrate metabolism.

The identity of a hyperglycæmia-producing substance found in pancreatic vein blood of animals treated with

[1] *New England J. Med.*, 1957, 256: 742 (April 18).

growth hormone or insulin remains in doubt. This has been thought to be glucagon, but the substance does not produce its effect in animals subjected to sympathetic blockade, which suggests that it is similar to adrenaline rather than glucagon. An extraction procedure undertaken by Fodden and Read made it unlikely, however, that adrenaline or any related substance was implicated.

The effect of glucagon on the liver has shown more clearly how it induces hyperglycæmia. Glucagon increases the amount of active liver phosphorylase, and this in turn catalyses the rate-limiting reaction in the transformation of liver glycogen to glucose. The active phosphorylase present in liver cells is the balanced amount depending on the opposing reactions between the inactivation of phosphorylase by a specific phosphatase and the reactivation of the resulting "dephosphophosphorylase" by a phosphokinase system. By a phosphate transfer this phosphokinase reactivates the phosphrylase. Glucagon now would appear to stimulate some portion of the phosphokinase system. The peak of active phosphorylase activity is some ten to fifteen minutes after glucagon administration, and concentration is returned to normal or below normal in about half to one hour.

That glucagon apparently has extra-hepatic functions has been shown in studies demonstrating the effects on stomach, kidney, skin and muscle. Confirmed studies have shown that glucagon inhibits stomach contractions and relieves hunger. Preliminary studies show that it also produces a marked but transient decrease in the volume and acidity of gastric juice in man. Studies in which the fate of I^{131}-labelled crystalline glucagon was being followed showed that the rate of I^{131} urinary excretion as inorganic iodide was much higher than in controls receiving I^{131} iodide alone. Studies in dog and man were then undertaken, which showed that glucagon enhanced the renal clearance of sodium, potassium, chloride and inorganic phosphate, presumably by a direct tubular effect, as there was no increase in glomerular filtration rate and the effect was not due to hyperglycæmia, osmotic diuresis or non-specific protein action. The output of glucose in skin slices is enhanced by glucagon. Its action in muscle is still controversial. The only study undertaken with pure glucagon in physiological doses (described in a preliminary report) showed that glucose uptake was increased by glucagon in the rat diaphragm, and that insulin and glucagon together had a greater effect than either alone.

The influence of glucagon on carbohydrate metabolism is by no means settled; the picture emerging indicates that glucagon has a dual, integrated action on carbohydrate metabolism (*viz.*, mobilization of liver glycogen and enhancement of peripheral glucose utilization) and suggests that the body has a glucagon-insulin mechanism whereby it can greatly increase glucose utilization and at the same time maintain greater constancy of blood sugar level and liver glycogen content than is possible with either hormone alone. Thus it has been independently shown that glucagon does not inhibit peripheral glucose utilization in normal man, and in another study that it actually enhances this use. In the latter study it was shown that insulin and glucagon together had more effect than either alone. This action of glucagon could be demonstrated in the pancreatectomized dog, but not after hepatectomy. It was also found possible to augment the insulin effect on peripheral glucose utilization with glucagon in some diabetic patients. Any desired effect on arterial glucose levels could be obtained by varying the ratio of glucagon to insulin over a limited period. These experiments offer hope that combined use of glucagon and insulin may prove useful in the management of some diabetics, especially in those whose blood sugar levels fluctuate widely on insulin. The work quoted is strong evidence against the widely held views that glucagon is "insulin antagonist" and is important in the ætiology of diabetes. Many attempts with many methods have not produced the permanent diabetic state after chronic glucagon administration, the hyperglycæmia-glycosuria being always fluctuating and transient. In studies using more specific stains than the early silver stains, the ratio of 60% alpha to 40% beta cells was found to obtain in diabetics as in normal subjects, an increased ratio being reported in many non-diabetic persons.

Clinically glucagon has been used successfully to terminate insulin coma in schizophrenics. In 140 instances of insulin coma, glucagon in a dose range of 0·003 to 0·3 milligramme per kilogram of body weight was successful in terminating 95 out of 97 on intravenous injection, 19 out of 22 on intramuscular injection, and 7 out of 11 on subcutaneous injection without any untoward reactions. One untoward reaction only has been reported following intravenous injection of 4·7 millilitres of glucagon (dose and preparation not specified). This reaction was one of marked hypotension occurring within a minute after an injection. A skin test later showed both insulin and glucagon sensitivity in this particular patient.

GLUCOSE MONOALEURITATE AS A NON-TOXIC INFUSION SUBSTANCE.

FOR many years there has been sought a non-toxic substance of high caloric value which could be used as an infusion substance. Fat emulsions prepared from natural fats and oils in many ways have been tried, but, in general, the emulsifying agents are more or less toxic. Soybean phosphatide, which was popular for a time, is precipitated by gamma globulins. Several water-soluble fatty acid derivatives, such as non-ionic detergents and emulsifying agents, have been tried, but these substances can be highly toxic. From a consideration of the reason for this toxicity, H. H. LeVeen[1] has introduced a new compound of glucose and aleuritic acid which he claims to be non-toxic on parenteral injection and available in the body as a food of high calorific value.

The emulsifying agents derived from fatty acids, such as the "tweens" and "spans", are toxic because of their surface active properties. Surface activity resides in the physical configuration of the molecule. The molecule contains a long fat-soluble portion and a water-soluble portion, non-polar and polar portions respectively. The fat-soluble part of the molecule dissolves in a lipid interface, and the water-soluble part tends to pull the lipid into the aqueous phase. Soaps act in this way, because the long hydrocarbon chain is lipophilic, and the sodium salt of the carboxy group is hydrophilic. When these surface-active substances are introduced into the blood-stream, they tend to pull the lipid portion of the cell membrane off the cell; hence the hæmolysis which commonly occurs after their use. The introduction of hydroxyl groups into the fatty-acid chain can produce substances which are not surface-active, for the hydroxylated fatty acid chain may have a greater affinity for water than for fat. Such a substance is glucose monoaleuritate. Aleuritic acid is a tri-hydroxy-palmitic acid which is one of the major ingredients of shellac. This compound has a molecular weight of 467, and because of its large molecular size a 13% solution is isotonic with a 5% glucose solution. One gramme would yield 6·24 Calories—that is, it is midway between glucose and fat.

This substance was prepared and given to rats on a fat-free diet with insufficient Calories, and the rats grew well; so the substance is metabolized quite adequately.

Parenterally injected glucose-l-aleuritate can then be isocalorically substituted for dietary fat with no apparent changes in the nitrogen balance and weight gain of a subject on a diet otherwise insufficient in Calories. No toxic symptoms were produced, nor did hæmolysis occur. The substance has not yet been tried on humans. All one can say at present about it is that if it can be made in sufficient quantity, it will probably be a very useful substance when parenteral nutrition is needed. It is, at least, an ingenious method of overcoming the present difficulties in the use of fat emulsions for intravenous injections.

[1] *Am. J. Clin. Nutrition*, 1957, 5: 251 (May-June).

Abstracts from Medical Literature.

SURGERY.

The Use of Jejunum to Replace the Stomach.

E. FREE, H. MANNIX AND J. BEAL (*Ann. Surg.*, December, 1956) discuss a series of 25 patients who were subjected to total gastrectomy for cancer of the stomach. In these patients, gastro-intestinal continuity was restored by means of a segment of jejunum, which was interposed between the œsophagus and the duodenum. Three deaths followed this operation, as well as 11 complications—namely, two cases of thrombophlebitis, two of a leak at the œsophago-jejunostomy, one of ileus, one of obstruction of the jejuno-duodenostomy, one of subcutaneous emphysema, one of pneumonia, one of wound infection, one of auricular fibrillation and one of depressive psychosis. Ten patients survived for more than six months after operation and have been evaluated in relation to gastro-intestinal function. Consequently the authors believe that the use of the segment of jejunum appears to have a favourable influence upon the course of the patient after total gastrectomy.

Carcinoma of the Œsophagus.

R. MUSTARD AND O. IBBERTSON (*Ann. Surg.*, December, 1956) review a series of 381 patients with carcinoma of the œsophagus admitted to the Toronto General Hospital from 1937 to 1953 inclusive. In this series there were 242 men (63·5%) and 139 women (36·5%). The average age was 62·9 years with a slightly younger age incidence in women. The maximum concentration of the tumours per unit of area was in the hypopharynx. From the whole series, only eight patients (3%) survived five years; four had a carcinoma in the hypopharynx, and two had an adeno-carcinoma of the abdominal part of the œsophagus, whereas one only had a squamous cell carcinoma of the thoracic part of the œsophagus. Of 87 "untreated" patients only two lived for two years, whereas none survived two and a half years. Of 76 patients receiving palliative treatment (jejunostomy or gastrostomy), only six survived for one year, and only one of these lived beyond two years. As a result of this, the authors question the value of gastrostomy for symptomatic relief or prolongation of survival. They prefer a substernal by-pass procedure, using either jejunum or colon to restore the ability to swallow. Of 125 patients in whom the primary tumour was treated only with high voltage radiation therapy, there was only one five-year survivor, and this patient had a squamous carcinoma of the posterior wall of the hypopharynx. Experience with patients treated since 1953 by the cobalt "bomb" has been somewhat more favourable. It was the authors' impression that most patients treated this way received at least temporary palliation, while a few had their primary tumour obliterated. Since the successful results of surgical treatment were so few, the authors believe it important to continue to explore the value of radiation therapy in this disease. Of the 381 patients in this series, only 133 were subjected to surgical attack, and resection was accomplished in 100 instances. Hospital deaths following operation totalled 48 (36·1%). The five-year survival rate of those surviving the completed excision and reconstruction of the œsophagus was seven out of 36. As a result of their observations the authors are sceptical of the chances of increasing the five-year survival rate by more radical excision. They consider that the main objective in regard to surgical treatment of these patients should be a reduction of operative mortality by a more careful selection of cases for exploration and more prompt recognition of non-resectability. They wish to explore fully the ability of cobalt radiation therapy to provide temporary palliation in those cases considered unsuitable for excision. Palliative surgical management should consist of a by-pass procedure to restore swallowing, whereas gastrostomy should be reserved as a last resort when all other measures have failed or are contraindicated.

Hæmorrhage as a Complication of Gastro-Enterostomy.

W. MYLAND, L. BARTHOLOMEW AND D. FERRIS (*Ann. Surg.*, December, 1956) report on a series of 1611 patients who had gastro-intestinal hæmorrhage and who were observed at the Mayo Clinic in the ten-year period from 1945 to 1954 inclusive. One hundred (6·2%) had undergone gastro-enterostomy previously. Gastro-jejunitis or gastro-jejunal ulcer was responsible for the hæmorrhage in at least 72% of the 100 patients. Bleeding following gastro-enterostomy was of greater magnitude than previously recognized, as 35% of the patients in this series were classified as having had a severe hæmorrhage. The authors state that bleeding may occur as a late sequel of gastro-enterostomy, as 45% of the patients had a hæmorrhage ten or more years after operation.

Leucoplakia and Carcinoma in Situ of the Lower Lip.

F. PALETTA, K. COLDWATER AND F. BOOTH (*Ann. Surg.*, January, 1957) discuss 65 cases of leucoplakia of the lower lip. They consider that this is not a benign lesion, and advocate that in such cases the whole area of the lower lip should be removed by what they describe as a "lip shave". "Lip shave" should accompany V-excision when the vermilion adjoining a malignant lesion contains areas of leucoplakia. Of the patients, 55 smoked cigarettes or a pipe, and 51 were farmers or worked outdoors. The operative technique of their "lip shave" was that the entire vermilion area of the lip was outlined with methylene blue. This area was then excised, the mucous membrane and the submucous layer down to the *orbicularis oris* muscle being included in the excision. The mucous membrane forming the oral surface of the lower lip was undermined, removed anteriorly and sutured to the skin to form the new vermilion border. The authors have followed-up 65 patients from three to five years; there has been no recurrence or development of a new lesion. They hold that leucoplakia of the lower lip should not be managed by patchy excision or random cauterization. Total excision of the vermilion and vermilion border is the best procedure, because of the tendency of leucoplakia to give rise to multicentric carcinoma. Moreover, in 12% of these cases clinically diagnosed as leucoplakia, they found *carcinoma in situ*, and they state that this certainly justifies the "lip shave" procedure. When on an area of the lower lip carcinoma has developed, a V-excision is the conventional method of treatment, the neighbouring mucous membrane being left alone. However, they consider that this neighbouring mucous membrane frequently is in some stage of leucoplakia, and that it is merely a matter of time until an obvious malignant lesion develops requiring another V-excision. Therefore, they remove the rest of the vermilion area of the lower lip by a "lip shave". They consider that surgery is preferable to radiotherapy in lesions of the lower lip.

After-effects of Gastrectomy.

A. MEDWID, J. WEISSMAN, H. RANDALL, H. BANE, K. ROBERTS AND P. VANAMEE (*Ann. Surg.*, December, 1956) confirm the results of previously reported work on patients after total gastrectomy, to the effect that the ingestion of hypertonic solutions or of carbohydrate meals results in a decrease in blood volume and electrocardiographic changes which coincide with the signs and symptoms of the "dumping" syndrome. They state that protein foodstuffs were quantitatively less effective than carbohydrate in producing the cardio-vascular alterations and the "dumping" symptoms. A diet with a low carbohydrate, moderate fat and high protein content, given at frequent intervals, resulted in weight gain and partial relief of the symptoms in these patients.

Water and Sodium Metabolism During Operation and Convalescence.

M. HAYES, R. WILLIAMSON AND W. HEIDENREICH (*Surgery*, March, 1957) have studied the endocrine mechanisms involved in water and sodium metabolism during operation and convalescence and conclude that trauma influences hypothalamic centres through the media of various neural effectors and possible humoral mediators. By disturbance of the usual homœostatic mechanisms operating in the hypothalamus, its effect on the pituitary gland is altered. By neural connexions, the posterior lobe of the pituitary discharges antidiuretic hormone. By probable humoral influences, the anterior lobe of the pituitary discharges at least thyrotropic and adrenocorticotrophic hormones, each acting on its specific target gland. These effects on the thyroid and adrenal cortex are antagonistic, and a new level of physiological equilibration is effected. Among the other metabolic effects of the increased release of adrenocortical steroids which are controlled by the anterior lobe of the pituitary is the possible increase in renal excretion of sodium, tending to a lowered serum sodium concentration. On the other hand, the authors state that the increased antidiuretic activity when water

is supplied too rapidly or in amounts beyond metabolic requirements results in primary water retention and serum dilution, leading to a lowered serum sodium concentration. The lowered serum sodium level, with an inadequate sodium intake, acts independently of any known controlling mechanism to increase adrenocortical release of aldosterone. This steroid effects maximal renal conservation of sodium. The authors state that the application of this theory should militate against the administration of amounts of water exceeding metabolic requirements. If the condition of sodium metabolism prior to trauma is not known with certainty, it probably would be unwise to give extra sodium during trauma and convalescence. If sodium depletion or restriction has not been operative before the traumatic episode, normal daily requirements of sodium can be given throughout operation and convalescence without fear of excessive retention and œdema.

Wounds of the Heart.

A. MAYNARD, M. AVECILLA AND E. NACLERIO (*Ann. Surg.*, December, 1957), as a result of their experience of penetrating heart wounds, have given up the use of pericardicentesis in hæmopericardium because the results were discouraging. They found, for instance, that when they were unable to withdraw blood at all, the pericardium might be full of clotted blood, and consequently in these cases they now perform an immediate thoracotomy with opening of the pericardial sac and removal of blood clot. They conclude that clotted blood in the pericardium can give rise to fibropericardium just like fibrothorax from clotted hæmothorax, and they consider also that this can give rise to a constrictive type of pericarditis.

Carcinoid Tumours of the Duodenum

Z. BARNES AND J. YOUNG (*Surgery*, November, 1956) report two cases of carcinoid tumours of the duodenum, one in which one carcinoid tumour caused symptoms of gastro-intestinal hæmorrhage, and one in which two carcinoid tumours were asymptomatic and were discovered at autopsy for another condition. In a review of the literature the authors were able to find a total of 26 cases of carcinoid tumours of the duodenum; 12 of these were symptomatic and the remainder were found incidentally. In most of the symptomatic cases there was a history of vomiting, upper abdominal pain and jaundice. In none was there gastro-intestinal bleeding except the one which they themselves reported.

Traumatic Rupture of the Dura.

T. MORLEY AND R. HETHERINGTON (*Surg., Gynec. & Obst.*, January, 1957) review 65 cases of dural tears associated with fractures of the paranasal air sinuses, the middle ear and mastoid air cells. As a result of their review of these patients, the authors consider that, when undoubted evidence exists of traumatic rupture of the dura in these situations, dural repair should be undertaken. They state that this fact applies to dural tears associated with middle ear and mastoid fractures as well as to those associated with fractures of the anterior fossa. The risk attached to an exploratory craniotomy is slight, but the chance of fulminating meningitis developing sooner or later in the untreated cases is considerable. Repair of torn dura with *fascia lata* is effective in preventing meningitis and in curing a cerebro-spinal fluid fistula or pneumocephalus.

Cancer of the Breast.

T. WATSON (*Surg., Gynec. & Obst.*, January, 1957) reviews 629 patients with cancer of the breast observed at cancer clinics from 1944 to 1954. As a result of operation a crude five-year survival rate of 48·3% was obtained in all new cases. The treatment policy in general for operable cases has been radical mastectomy and post-operative X-ray therapy. The author considers that this series from the point of view of selection was similar to McWhirter's and shows a superior crude five-year survival rate. He also states that he has demonstrated that, providing the published data on the survival of untreated breast cancer are representative, treatment favourably influences the course of the disease.

Carcinoma of the Maxillary Sinus.

R. POLLACK (*Ann. Surg.*, January, 1957) discusses 31 cases of carcinoma of the maxillary sinus. He states that carcinomata of the nasal cavity and paranasal sinuses comprise about 0·2% of all malignant tumours. At least 80% of these lesions arise in the maxillary sinus. The author has found that most patients with antral cancer come for treatment in an advanced stage of the disease, which makes the treatment of these conditions a difficult therapeutic problem. However, he states that distant metastases are rare. The method of treatment in these cases was by surgical excision, so that a wide-open, clean cavity without overhanging edges or pockets was left, and this was followed-up by deep X-ray therapy. In 31 cases most of the tumours were epidermoid in type. In 22 cases the stage of the disease was advanced. However, of the total group, 13 patients showed no evidence of recurrence of disease between one and five years after operation.

A Single Transverse Incision for Radical Neck Dissection.

J. ATTIE (*Surgery*, March, 1957) performed a complete neck dissection through a single transverse incision low in the neck, with excellent exposure and improved cosmetic appearance. The author considers this the ideal incision, as longitudinal incisions of the neck are prone to keloid formation.

Primary Closure of the Common Bile Duct After Exploration.

J. HERRINGTON, R. DAWSON, W. EDWARDS AND L. EDWARDS (*Ann. Surg.*, February, 1957) point out that closure of the common bile duct (primary choledochotomy) as opposed to T-tube or catheter drainage has been employed infrequently by surgeons in the United States of America. However, over the past ten years the authors have closed the common duct after its exploration in 153 cases. Post-operative morbidity was less in another 89 cases in which T-tube or catheter drainage was employed after exploration of the common duct. They state also that at present closure of the common duct following exploration is being employed with increasing frequency in the surgical service of the Vanderbilt University.

Chronic Hypokalæmia After Total Gastrectomy.

D. SENSENIC AND R. CAMPBELL (*Ann. Surg.*, January, 1957) review a series of 22 patients who underwent total gastrectomy. They observed in two cases, probably in a third, and possibly in a fourth, a condition of chronic hypokalæmia, which they consider caused sudden death in the first, second and fourth cases reported in this paper. They consider that special attention must be paid to this condition in patients who have undergone total gastrectomy. If chronic hypokalæmia develops, prompt efforts should be made to correct the condition and prevent its recurrence.

Syme's Amputation.

R. I. HARRIS (*J. Bone & Joint Surg.*, August, 1956) discusses the differences of opinion as to the use of Syme's amputation expressed by military surgeons in Canada, Great Britain and the United States of America. He refers back to Syme's original record published in 1843, twenty-three years before Joseph Lister's experiments in antiseptic surgery, and three years before the administration of the first ether anæsthetic at the Massachusetts General Hospital. Syme's concern was a simple and safe method, and his success indicated the safety of his method in an era when infection was most common. The author points to Syme's second consideration that the method provided "a stump seemly and useful for support and progressive motion". This allows for the important fundamental principles of end-bearing amputations. The lower extremity propulses and bears weight. Weight bearing is best when the stump is end bearing. Propulsion is best performed by lengthening normal functioning joint and muscles above the amputation. Essential requirements for end bearing are: (i) A cross section as great as possible to give a broad area of support. (ii) Ability of the whole cut surface of bone to bear weight; this is achieved with cancellous bone, or in the ankle by retaining subarticular cortical bone at the lower end of the tibia. (iii) Appropriate skin and subcutaneous tissues. Only two areas meet these requirements—the lower end of the femur covered by prepatellar skin, and the expanded ends of tibia and fibula covered by a heel pad. The author lists the advantages of this method: the stump takes full weight, and this ability is retained to the end of the patient's life; the stump is of nearly normal length; the patient can stand for long periods, undertake heavy work, and walk even without a prosthesis. The author states that the main disability from this method is the broad base and the unsightly prosthesis. The position has been improved by the use of plastics. The author discusses the operative technique in detail.

Clinico-Pathological Conferences.

A CONFERENCE AT SYDNEY HOSPITAL.

A CLINICO-PATHOLOGICAL CONFERENCE was held at Sydney Hospital on March 19, 1957, DR. J. REIMER, the Assistant Medical Superintendent, in the chair. The principal speaker was DR. G. MICHELL, who was Senior Registrar at this hospital in 1956.

Clinical History.

The following clinical history was presented.

The patient was an accountant, aged twenty-eight years, who had been discharged from the army with symptomless hypertension two years before his admission to hospital. He was under the care of a physician for about a year before his admission, and the records showed that he then complained of frontal headaches present for two years and of fatigue of recent onset. His vision was normal. At that time his general physical condition was noted as excellent and he was perspiring freely. Other findings were as follows: his height was five feet nine inches, his weight was 159 pounds, his blood pressure was 250/170 millimetres of mercury, and the apex beat was in the fifth left intercostal space five inches from the mid-line. The second heart sound was accentuated. Papilloedema was present in both eyes. The urine was acid, with a specific gravity of 1·020. No other abnormality was found. The visual acuity was normal.

The patient was unwilling to submit to sympathectomy. He was examined at frequent intervals, with the following findings. In June he had no complaints. Papilloedema with striate hæmorrhages and patches of exudate were present in both retinæ. His blood pressure was 200/160 millimetres of mercury. In July he complained of increasing fatigue. Triple cardiac rhythm of the protodiastolic type was present to the left of the lower end of the sternum. His blood pressure was 200/140 millimetres of mercury. In August his main complaint was headache. There was a cloud of albumin in his urine. In September his headaches remitted; his vision was slightly blurred. In December protodiastolic cardiac rhythm was still present. Papilloedema of four dioptres was present and there was a cloud of albumin in his urine. His blood pressure was 210/150 millimetres of mercury. In January the headaches were again present, but were less severe than formerly. His urine contained a heavy cloud of albumin. His blood pressure was 190/160 millimetres of mercury. In February there was a faint cloud of albumin in the urine. His blood pressure was 190/110 millimetres of mercury. In March, quadruple cardiac rhythm was present. There was a heavy cloud of albumin in his urine. Star-shaped exudates were seen in the macular region. His blood pressure was 200/160 millimetres of mercury.

The patient was admitted to Sydney Hospital one month later, complaining mainly of sleeplessness, ankle swelling, breathlessness on exertion and frequent bouts of vomiting. In addition he now had cramp in his legs, palpitations and lumbar pain, and his vision had become much worse. He had lost his appetite, and often sweated profusely and became flushed. His past history included only childhood exanthems and whooping-cough. His father had died at the age of fifty-five years from hypertensive cardiac disease, and his mother, brothers and sisters were alive and well.

Physical examination of the patient showed him to be breathless, flushed and sweating. The pulse rate was regular at 126 per minute. The vessel wall was not palpable. The apex beat was in the sixth left intercostal space, six inches from the mid-line. There was gallop rhythm. The second sound was accentuated in all areas. No murmurs were heard. Respiration was of the Cheyne-Stokes type. Apart from a few crepitations at the bases of the lungs the respiratory system was normal. The liver was tender and enlarged to two inches below the right costal margin. No other masses were felt in the abdomen, but tenderness was present in the loins. Examination of the central nervous and hæmopoietic systems revealed no abnormality. Examination of the fundi revealed papilloedema with blurring and distortion of the disks, and macular stars. The urine contained a heavy cloud of albumin, and its specific gravity was 1·010. During his stay in hospital there was an irregular, remittent fever, the temperature reaching 100° to 101° F., and the pulse rate was constantly elevated to about 120 per minute. The results of special investigations were as follows. The blood urea nitrogen content was 11 milligrammes per 100 millilitres and the blood creatinine content one milligramme per 100 millilitres; the urea clearance (standard) was 135%. A urea concentration test gave the following figures: before urea, 2·7 grammes *per centum*, 103 millilitres; one hour after, 3·1 grammes *per centum*, 110 millilitres; two hours after, 2·9 grammes *per centum*, 60 millilitres; three hours after, 2·4 grammes *per centum*, 54 millilitres. Microscopic examination of the urine was performed once, and revealed an occasional pus and red cell and occasional hyaline and granular casts. No growth was obtained on attempted culture. The hæmoglobin value was 13·6 grammes *per centum*; the white cells numbered 17,500 per cubic millimetre (neutrophils 82%, lymphocytes 18%).

On the fifth day in hospital he was dyspnœic, and his blood pressure was 154/142 millimetres of mercury. Next day he was cyanosed and had many crepitations at the base of the right lung. Shortly before his death on the tenth day he had dusky cyanosis and pronounced orthopnœa. The pulse was regular, the blood pressure was 220/200 millimetres of mercury, and the apex beat was in the sixth left intercostal space six and a half inches from the mid-line. There was œdema of the sacrum, but not of the ankles, and the liver was tender and enlarged to two fingers' breadth below the costal margin. The patient had been treated only with sedation and, terminally, with morphine and oxygen.

DR. J. REIMER: Ladies and gentlemen, I welcome you to the third clinico-pathological conference of the 1957 series and introduce Dr. George Michell, who is to give us the presentation of the case today.

DR. G. MICHELL: Before commencing the discussion of the possible diagnosis in today's case, I will ask you to bear with me for a few minutes while I go over the salient features of the patient's history.

The patient was a male and was twenty-eight years of age when discharged from the army because of hypertension. When he was examined a year following his army discharge, which was one year prior to his death, he complained of frontal headaches of two years' duration, and of fatigue of recent onset. He was neither overweight nor underweight. Gross hypertension was found, the blood pressure being recorded as 250/170 millimetres of mercury. His heart was enlarged clinically and no murmurs were detected. The visual acuity was normal, though bilateral papilloedema was found. No abnormal constituents were found in the urine, and the specific gravity (apparently of a random sample) recorded was 1·020. It was also noted that he was perspiring freely. He refused to have a sympathectomy. He was examined at frequent intervals over the next eleven months, and we are presented with the picture of gradual deterioration of health. The degree of hypertension is unchanged. The onset of abnormal triple and quadruple rhythms indicates that the myocardium is failing. Exudates appear on the retina and visual acuity is deteriorating. At the same time, albuminuria appears. One month later, the patient was admitted to hospital in a terminal state. He complained of exertional dyspnœa, dependent œdema, sleeplessness and vomiting. His vision had deteriorated further. He also complained of often sweating profusely and becoming flushed. His past history included only childhood exanthemata and whooping-cough. His father had died from hypertension at the age of fifty-five years; his mother and siblings were alive and well.

On examination, he was flushed, sweating, and had the Cheyne-Stokes type of respiration. The heart had enlarged further, gallop rhythm was present, and, as on previous examinations, no murmurs were audible. Crepitations were heard at the lung bases, and the liver was enlarged and tender. Papilloedema and retinal exudates were present as previously. Heavy albuminuria persisted, and the specific gravity of what I again assume to be a random specimen was recorded as 1·010. Over the next few days he developed orthopnœa, cyanosis, and many crepitations at the right lung base, and he died on the tenth day. An irregular remittent fever was recorded throughout his stay in hospital. Special tests performed in hospital demonstrated that there was no nitrogen retention in the blood, and renal function, as measured by the methods of urea clearance and urea concentration, was normal. A single examination of the centrifuged deposit of urine showed occasional pus and red cells and occasional hyaline and granular casts, and no growth on culture. The hæmoglobin value was within normal limits, and the white cells showed a neutrophil leucocytosis.

In summary, then, we have the story of a young man who had hypertension with bilateral papilloedema, and over a comparatively short period deteriorated, and finally died in congestive cardiac failure.

At this stage I will say a few words about bilateral papilloedema. Swelling of the optic nerve head may be due to optic nerve neuritis, to an intracranial space-occupying lesion, to the severe anoxia of anoxic pulmonary disease, or to hypertension. I will immediately dismiss optic nerve neuritis as the cause of the optic nerve œdema in this particular patient, because his visual acuity was initially perfectly normal, whereas optic nerve neuritis is characterized by gross diminution of visual acuity. In intracranial space-occupying lesions the blood pressure may be compensatorily raised; but I have never seen or heard of it reaching the fantastic heights reached in this patient for any length of time. Furthermore, our patient did not go on to develop any of the symptomatology of untreated cerebral tumour. Anoxic pulmonary disease can be ruled out on clinical grounds also. Therefore, it is quite reasonable to assume that the papillœdema in this case is due to the hypertension. Hypertension and papillœdema add up to make a diagnosis of the clinical syndrome of malignant or accelerated hypertension which I believe to be the basis of this patient's illness.

The syndrome of malignant hypertension is expressive of very severe arterial hypertension, and may be due to a multitude of causes. Clinically, it is characterized by very high blood pressure, hypertensive neuro-retinopathy, and in most cases, progressive renal failure. Without treatment, the prognosis is very poor. Pathologically, the characteristic lesion is necrotizing arteriolitis, most severe and widespread in the kidneys. We can therefore assume that necrotizing arteriolitis is present in patients who have the syndrome of hypertension and papillœdema. To this broad statement there is one fundamentally important exception, which I will discuss later.

A discussion of the evolution of medical thought concerning the pathogenesis of necrotizing arteriolitis since its first description by Volhard and Fahr in 1914 is most fascinating, but beyond the scope of today's discussion. Suffice it to say that most modern workers in this field now consider that this arteriolar lesion is related to the degree of hypertension, and the speed with which it is attained. As the blood pressure rises, the severer grades of change appear and increase in frequency. This is particularly notable for the necroses which begin to appear with a diastolic pressure of 150 millimetres of mercury, and become more frequent as the pressure rises. The arterioles are thought to be destroyed mechanically by the high blood pressure. Thus, without going into details, there is fairly convincing evidence for the view that arteriolar necroses in human malignant hypertension are a consequence of the level of arterial pressure, a hypothesis which is further supported by the demonstration that the malignant phase may be reversed to the benign if the blood pressure is lowered.

The great majority of patients with hypertension belong to the group which, in our present state of ignorance, we call essential. We classify hypertension as essential when we are unable to incriminate any specific cause.

On the whole, our patient's initial presentation and the mode of clinical progress of the disease are consistent with the diagnosis of essential hypertension in the malignant phase; but there are one or two most puzzling features which I think make the diagnosis untenable. As I have stated earlier, the essential histological lesion of this disease is necrotizing arteriolitis, and it is the arterioles of the kidneys which bear the main brunt of the attack, leading usually to microscopic and often macroscopic hæmaturia and progressive azotæmia. The evidence, as I interpret it, is against this patient having renal damage typical of this lesion. The patient had albuminuria for nine months prior to his death. But albuminuria is common in hypertension and in congestive cardiac failure, and its presence does not imply severe renal damage. On his terminal admission to hospital, the specific gravity of this man's urine was recorded as 1·010. The measurement of the specific gravity of urine is worthless as a measure of the kidney's ability to concentrate. Only if a patient is deprived of water over a period of many hours are we in a position to draw any conclusions, and this was not done in this case. Only one microscopic examination of the urine is available, and this shows occasional pus and red cells, and occasional hyaline and granular casts. Even if urine is not examined until several hours after it is passed, it is not usual for pus and red cells to break up, and therefore we can assume that the number of these cells is within normal limits. I can explain the presence of hyaline and granular casts on the basis of hypertension alone, without necrosis of the renal arterioles, and besides, they are common in congestive cardiac failure from any cause, presumably owing to the raised venous pressure. Nor is there any azotæmia, the blood urea nitrogen and creatinine figures being well within normal limits. The standard urea clearance figure of 135% is perfectly normal. I will admit that the maximal urea clearance is preferable to the standard, but there is nothing wrong with this figure. Also, the kidney can concentrate urea quite normally, the figures ranging from 2·4 to 3·1 grammes *per centum*.

It is difficult to believe that a patient can have such excellent renal function if there is concomitant necrosis of his renal arterioles, especially in the terminal stages of the disease. I cannot completely reject the view that this patient was suffering from essential hypertension in the malignant phase, and must consider it a possibility; but I feel that the weight of evidence against it is rather heavy.

The next possibility, the congenital lesion, coarctation of the aorta, is the next condition I will consider. Incidentally, I would like to remind students present here today that to omit the palpation of the femoral arteries in a patient with hypertension is a cardinal medical sin.

Points against our patient having this disease are: Firstly, I think his blood pressure would have been measured prior to his entrance in the army, and the presumption is that it was then normal. Secondly—and I feel that this is the most decisive point—the malignant phase in coarctation occurs only very, very rarely. The only case of coarctation of the aorta associated with papillœdema that I know of was written up by Cleland and his colleagues in August last year. In this case, incidentally, the papillœdema disappeared following surgical resection of the coarctated area. Thirdly, death from congestive heart failure in coarctation is relatively uncommon, it tends to occur in the older age groups, and is most often associated with valvular abnormalities. Fourthly, apart from the collateral channels which are usually visible and audible around the scapulæ of these patients, systolic murmurs are almost invariably heard over the precordium due to the enlarged internal arteries, and no murmurs were detected in the patient under discussion.

Of the next group of diseases which cause hypertension, chronic renal disease, the first condition I will discuss is that of chronic bilateral pyelonephritis, which is the commonest renal lesion causing hypertension. In most cases of this disease there is some history of an acute episode, and recurrent urinary symptoms are fairly common. Furthermore, pus cells are almost invariably found in the urine, and renal function is impaired. None of these features are found in our patient, and I feel that this diagnosis can be confidently excluded.

The next renal condition is chronic glomerulonephritis. There is no history of an acute episode, although admittedly some chronic nephritics give no history of acute nephritis. The good renal function found in our patient is sufficient to rule out this diagnosis.

Polycystic disease of the kidneys is a disease characterized by a long course, punctuated by bouts of hæmaturia, pain and renal infection, and the end stage is usually dominated by renal failure. An abdominal tumour can usually be felt. In addition, the malignant phase very rarely supervenes in the hypertension of this condition, and it need not be considered any further.

Other rare causes of bilateral renal disease causing hypertension, such as irradiation nephritis, renal artery occlusion *etc.*, I will not discuss. Nor will I discuss the Kimmelstiel-Wilson syndrome which occurs in diabetes.

Unilateral renal disease may be another cause of hypertension. It is of great importance clinically, because in some cases surgical removal of the diseased kidney may result in cure of the hypertension. Therefore, an excretion urogram is now mandatory in the investigation of our hypertensive patients. If unilateral renal disease is found in the intravenous pyelogram, further investigation is indicated; so retrograde pyelography and differential renal studies are carried out, firstly to determine the ætiology, and secondly to estimate the degree of function in each kidney. The most important of these unilateral lesions is pyelonephritis, because it is by far the commonest lesion in which removal of the diseased kidney may be followed by cure of the hypertension. The following points about this disease are emphasized in the literature. Firstly, in most cases it is symptomless, and there has been no previous history of renal infection. It is only found on routine pyelography. Secondly—and this is most important—pus cells are often not found in the urine, because in many cases the diseased kidney is completely functionless. And thirdly, hypertension, in either the benign or malignant phase, may be cured following surgical excision of the diseased kidney, provided always that the contralateral kidney is completely free of infection.

I do not think that this disease was present in our patient, because of the normal renal function found terminally. As I have already stated, it is difficult to imagine the process of necrotizing arteriolitis going on in the kidneys—and in this case it would be in the remaining kidney—without gross renal dysfunction being evident.

There are many other cited causes of unilateral so-called surgical renal disease which may cause hypertension. The commonest causes are said to be calculous hydronephrosis, calculous pyelonephrosis and various anomalies of the branches of the renal artery. These conditions, in contrast to unilateral pyelonephritis, are usually associated with some history of renal disease. For this latter reason, and the reasons I have mentioned earlier, we may exclude these lesions from the possible diagnosis.

The next group to be discussed, although very briefly, is the group of so-called collagen diseases. *Polyarteritis nodosa* is an inflammatory and necrotizing lesion of the small and medium-sized arteries. It is of great theoretical interest, because the arteriolar lesions resemble somewhat the necrotizing arteriolitis of malignant hypertension, though its pathogenesis seems to be totally different. Since blood vessels may be involved anywhere in the body, it usually presents as a disease involving many systems. Time does not permit a detailed discussion of its symptomatology, but suffice it to say that the only symptom which may be suggestive of the disease is our patient's complaint at one stage that he had cramps in his legs. I do not for one moment think that this was suggestive of a polyneuritis, and these cramps may be easily explained on the basis of the patient's sweating attacks *plus* the fact that he was almost certainly advised to restrict his salt intake. The other collagen disease which may cause hypertension, disseminated *lupus erythematosus*, occurs almost exclusively in women, and there are no symptoms or signs to support this diagnosis in the case under discussion.

Lead poisoning as a cause of hypertension can also be rejected. Acute lead poisoning may cause an encephalopathy with papilloedema and a temporary compensatory rise in blood pressure. Chronic lead poisoning is cited as a cause of hypertension, either benign or malignant, and this appears to be secondary to the chronic nephritis which can follow exposure to lead over long periods.

The last group I have listed here is the endocrine one. I will very quickly discuss the less common of these endocrine conditions before discussing chromaffin cell tumour.

Cushing's syndrome, first described in 1932, may be due to a microscopic pituitary basophil adenoma causing bilateral adrenal gland hyperplasia, or else it may be due to an adrenal gland adenoma or carcinoma. Females predominate over males in the ratio of three to one, and its well-known manifestations are quite easily understood if we recall the symptomatology of cortisone overdosage. The hypertension in this condition tends to be severe, and the malignant phase is by no means uncommon. In our patient there is no suggestion of a rapidly acquired and painful adiposity, confined to face, neck and trunk, no purplish striæ, no suggestion of osteoporosis causing backache, and kyphosis *etc.*, and apart from the hypertension there is no clinical feature suggestive of this syndrome.

Primary aldosteronism is a complex syndrome first described by Conn in 1955, and appears to be due to the excessive production of the potent sodium-retaining, potassium-excreting corticoid, aldosterone. In most cases it is due to an aldosterone-secreting adrenocortical adenoma, though bilateral hyperplasia of the adrenals may also cause this syndrome, and cure may follow subtotal adrenalectomy. Excessive potassium is lost in the urine, and the subsequent hypokalæmia causes a tubular lesion resulting in polyuria and hyposthenuria. Conn's syndrome is suggested in a hypertensive patient if there is a history of periodic severe muscular weakness due to low serum potassium, intermittent tetany and paræsthesiæ due to the alkalosis, polyuria, persistently alkaline urine and hypernatræmia. There is little to support this diagnosis in either our patient's history or good renal function.

For the sake of completeness I will say a few words about carcinoid tumour of the intestine, the generalized effects of which appear to be due to the humoral effect of 5-hydroxytryptamine or serotin. Apart from the history of flushing, there is nothing else to suggest this diagnosis in today's case. The patient has no abdominal or respiratory symptoms, and no sign of organic pulmonary valvular stenosis. Furthermore, I was not able to find any reference in the literature to a case of malignant hypertension associated with carcinoid. And the hypertension associated with carcinoid is mild.

Chromaffin-cell tumour, otherwise known as paraganglioma or phæochromocytoma, is a tumour of secretory tissue containing, in varying proportions, abnormal quantities of the sympathetic nervous transmitters, adrenaline and nor-adrenaline. These substances may enter the bloodstream in paroxysms and cause hypertensive crises of the most frightening nature, or else they may be the cause of persistent hypertension in a benign or malignant phase. These tumours, though uncommon, should always be borne in mind as a cause of hypertension, because their successful surgical resection may result in cure of the disease.

Histologically, the tumours are usually benign, but occasionally malignant. They most frequently arise in the adrenal gland, more commonly on the right side than the left, and occasionally they are bilateral. They can also arise from any part of the sympathetic nervous system. An abdominal tumour is said to be palpable in about one-third of cases.

Frankel in 1886 described his findings, at post-mortem examination, of bilateral adrenal tumours and cardiac hypertrophy in an eighteen-year-old girl, who during life had attacks of palpitations, headaches and vomiting. The first clear clinical recognition of this condition was in 1922 by Labbé, Tinel and Doumer. Mayo, in 1927, was the first surgeon to excise one of these tumours successfully.

Paroxysmal attacks are characterized by one or more of the following symptoms: nausea, a sinking feeling in the epigastrium, epigastric pain, vomiting, palpitations, retrosternal pain, throbbing in the temples, headache, dizziness, sweating, a feeling of coldness or "goose-fleshiness", or a coarse tremor. The patient may appear anxious, the skin is blanched or mottled and cold to the touch. Profuse and drenching sweating is common. The pupils are dilated, the neck veins are often distended, and occasionally the thyroid gland has been observed to be swollen during an attack. The blood sugar is raised, and glycosuria is often present. The body temperature is elevated in many cases. The blood pressure rises steeply from the vasoconstrictor action of these hormones.

As mentioned earlier, adrenaline and nor-adrenaline are released in varying proportions. Investigations over the past few years indicate that their proportions may be taken as a rough guide to the location of the tumour. For instance, with adrenal tumours, much greater quantities of adrenaline than nor-adrenaline are produced. With tumours situated elsewhere in the sympathetic nervous system, greater quantities of nor-adrenaline are released into the circulation. Clinically, the different effects of these hormones are most easily appreciated from their effects on the heart. If equal amounts are secreted, then the effects of adrenaline predominate, and only when the tumour secretes more than 75% of nor-adrenaline do the effects of the latter hormone manifest themselves.

The heart rate and rhythm depend on whichever hormone has the predominant effect. With adrenaline, which has a direct excitatory action on the myocardium, tachycardia is usual and extrasystoles are frequent. Nor-adrenaline, on the other hand, has no direct action on the myocardium. If this is the preponderant hormone, bradycardia occurs reflexly owing to stimulation of aortic and carotid baroreceptors, and ectopic beats do not, as a rule, occur. The attacks are of variable duration, lasting from a few minutes to several days. The patient may die in one of these attacks, usually of acute pulmonary œdema, occasionally of cerebral hæmorrhage, and occasionally of peripheral circulatory failure after the attack has passed off.

Our patient did not have paroxysmal attacks of hypertension, but I feel that the foregoing discussion was worth while, because in chromaffin-cell tumour we have the only example of hypertension in which we have even a remote acquaintance with the mechanism. Chromaffin-cell tumour may also be the cause of persistent hypertension, in either the benign or malignant phase, and I believe this to be the probable diagnosis in this patient.

Even in persistent hypertension caused by this tumour, paroxysmal attacks may occasionally occur which may be comparatively slight and have nothing in their content to suggest the presence of this tumour. Smithwick *et alii* in 1950 analysed the findings in 11 cases in which such tumour was found at operation for sympathectomy, the diagnosis having been unsuspected before operation. Smithwick emphasizes the frequency of excessive sweating, vasomotor phenomena, an elevated body temperature, elevated basal metabolic rate and glycosuria in these tumours, and their rarity in essential hypertension.

Now to return to our patient. Sweating is emphasized in the protocol, both as a symptom and as a sign. But we are told that the patient is flushed, and I have already stated that the skin is usually blanched or mottled. Nevertheless, flushing of the face is fairly common, though the limbs may be blanched, and generalized flushing occurs following a paroxysm of sweating, so flushing is not inconsistent with the diagnosis. Our patient had no other vasomotor phenomena, and sugar was not detected in his urine. The only reference we have to pulse rate is on his terminal admission, and the heart failure alone could explain the tachycardia. He had an irregular, remittent fever on his terminal admission—this may be significant, but the râles in his lungs may have been the cause of his fever. So far, therefore, the only positive diagnostic feature is the sweating.

But I base my diagnosis on one further irrefutable fact, and that is that this patient had no significant renal damage. It is quite extraordinary, and a fact for which I can find no satisfactory explanation, that in chromaffin-cell tumour alone, of the types of lesion causing malignant hypertension, there is a dissociation between the clinical sign, hypertensive neuro-retinopathy, and the histological sign, arteriolar necrosis. In other words, these patients have papillœdema and hypertension, the combination which we call malignant, but the essential histological feature of arteriolar necrosis is not found on examination of the organs; therefore renal function, which is so severely affected in other forms of malignant hypertension, remains normal in these cases. Albumin, casts and even red cells may be found in the urine; but renal function, as measured by the usual laboratory methods, remains unimpaired. In some cases urea retention has been described, but this has been explained by the vomiting. I might mention that in 1950 Platt and Davison wrote up a case of chromaffin-cell tumour where arteriolar necrosis was present, and to my knowledge this is the only exception. We can thus take it that necrosis does not occur except very rarely. Our patient did have albumin and occasional casts, but no other visible abnormality. Furthermore, as discussed earlier, he had no renal damage as measured by the methods of urea concentration and urea clearance; all of which is consistent with malignant hypertension associated with phæochromocytoma. Therefore, I will submit that we have here a case of clinical malignant hypertension with no arteriolar necrosis—a condition which only occurs, as far as I know, in chromaffin-cell tumour.

If the diagnosis in this case is correct, how could we have gone about proving it? I can only do this very briefly.

In this case no abdominal mass is palpable, but a plain X-ray film of the abdomen may have shown a soft-tissue shadow, and the intravenous pyelogram may have shown distortion and displacement of the kidney.

The next step is to use one of the adrenergic blocking agents of which the adrenolytic drug "Regitine" is the most popular and reliable: five milligrammes are injected intravenously, and if the diastolic pressure falls by more than 25 millimetres, then the result of the test is said to be positive. False-positive reactions may occur if the patient is taking a barbiturate drug, or if any nitrogen retention is present. Also, false-positive or false-negative results can occur without any apparent reason. The use of "Regitine" is good as a screening method, and should be tried in most hypertensive patients where the ætiology is obscure; but a negative result should not exclude the diagnosis if there is clinical suspicion of the disease.

Fortunately, the above test has been, or will be, superseded by a method of great precision, namely, the assay of catechol amines in the urine. Engel and von Euler, in 1950, showed that the rate of urinary excretion of adrenaline and nor-adrenaline was greatly raised in phæochromocytoma. This was initially a biological assay; but with the introduction of chemical methods of estimating these substances, there seems little doubt that the urinary excretion of the catechol amines will become the standard method of deciding whether or not a chromaffin-cell tumour is present.

Surgical resection carries a mortality of up to 30%. During the mobilization of the tumour by the surgeon the blood pressure may rise to astronomical heights, and the anæsthetist has to use "Regitine" to control this pressure. Following resection of the tumour, a profound fall in the blood pressure may occur, and nor-adrenaline infusion may be necessary over a period of several days.

Without further ado, Mr. Chairman, ladies and gentlemen, I will rest my case. I beleve that today's patient was probably suffering from hypertension in the malignant phase due to chromaffin-cell tumour. I am basing the diagnosis on our patient being a fairly typical case. I cannot with certainty exclude most of the other causes of hypertension I have mentioned, especially essential hypertension in the malignant phase; and if this is so, it is just another example to support a statement I heard only a few weeks ago—namely, "that it is the unexpected which makes clinical medicine so fascinating, the element of chance being much more prominent than in horse-racing or poker".

DR. J. REIMER: Thank you, Dr. Michell for a clear and comprehensive discussion of this case. I would like to congratulate you on your presentation. I now call on members of the audience to comment on the remarks made by Dr. Michell on any aspect of this case.

DR. K. B. NOAD: I, too, would like to congratulate Dr. Michell on his able discussion. Indeed it leaves little to be said. I quite agree with his interpretation of the protocol and I would say that this patient had a phæochromocytoma, always remembering that he might have two of them, one on each side. There is nothing else that I can say.

DR. W. L. CALOV: I must apologize for being late for this discussion, and in hearing the latter part of Dr. Michell's discussion I must say I was very impressed. I take it by the acclamation at the conclusion of his presentation that the earlier part of the discussion was just as impressive as the conclusion. I feel sure that he has the correct diagnosis, and agree that the patient had a phæochromocytoma. I assume that the man died of cardiac failure because of the great strain put on his heart by the blood pressure.

DR. K. D. G. EDWARDS: I would like to mention some tests which may determine whether this is a case of phæochromocytoma or possibly a case of primary aldosteronism. I think a chest X ray would be important, and the result of this has not been mentioned. About 15% of chromaffin-cell tumours show an opacity above the diaphragm in a plain X ray of the chest. I have recently seen such a case of a functioning tumour occurring in the chest and apparently cured by operation. As far as aldosteronism is concerned, an estimation of the serum and urinary electrolytes would be helpful and was not mentioned in this case. One would expect a low serum potassium and an excess of potassium in the urine with polyuria resistant to "Pitressin", and a defect in acid-base regulation. I do not think recurrent paralysis is a necessary feature, and the absence of this sign in this patient does not exclude the diagnosis of aldosteronism.

DR. J. REIMER: Professor Magarey, Dr. Michell mentioned the difficulty he found in a review of the literature in finding reference to necrotizing arteriolitis as occurring in phæochromocytoma. Would you care to comment on this aspect?

PROFESSOR F. R. MAGAREY: I have never heard of that lack of relationship between necrotizing arteriolitis and phæochromocytoma. It is of great interest.

DR. B. PASCOE: I would like to hear from Dr. Michell an opinion on the place of perirenal air insufflation in the diagnosis of phæochromocytomas.

DR. G. MICHELL: This is a fairly risky procedure, which may precipitate a paroxysm of very high blood pressure due to compression of the tumour. It is therefore usually discouraged, even though control is now possible by the use of "Regitine". For this reason, exploratory laparotomy is preferred. I might add that although chromaffin-cell tumours can be found anywhere along the sympathetic chain, the great majority are to be found in the abdomen.

DR. H. S. H. WARDLAW: I agree with Dr. Michell that if a simple test for phæochromocytoma were available it would be very useful. So far as I can ascertain, the biological estimation is still the most reliable, although it is not possible as a routine measure. The measurement of these pressor amines by means of their fluorescence in ultraviolet light has been very widely studied, particularly by the Scandinavians; but there are difficulties due to the occurrence of the two amines in varying proportions. They have very different pressor effects, nor-adrenaline being much more effective than adrenaline. But the fluorescence produced by nor-adrenaline is considerably less than that produced by adrenaline. Furthermore, interfering substances must be carefully got rid of. Quite recently my attention was called to an article describing a colorimetric method (Burn and Field, 1956). The authors claim that the method can be relied upon to exclude a diagnosis of phæochromocytoma, but they recommend that positive results be confirmed by biological assay. I have no doubt that the chemical and fluorimetric methods will in time be simplified.

DR. D. HANDLEY: I notice there is no mention of the femoral pulses in the protocol. Does Dr. Michell not consider them of importance?

DR. G. MICHELL: That is so, but I feel that even in the absence of this information, I can exclude coarctation of the aorta on other grounds.

DR. H. M. WHYTE: Judging from the protocol, this patient was in the hospital many years ago. In these days the patient would have lived longer with modern treatment, and would have given the clinicians more time to make a diagnosis. This could be accomplished by the use of ganglion-blocking agents. I think that this is one form of disease in which, no matter what the cause, treatment can prolong life to some extent.

DR. J. REIMER: I will call on Dr. Palmer to present the findings.

Autopsy Findings.

DR. A. A. PALMER: The patient had been a young man weighing 130 pounds, indicating a weight loss of 29 pounds in the last year of his life. The notable findings were as follows: (i) Bilateral suprarenal tumours. The right suprarenal gland was almost entirely replaced by an ovoid, encapsulated newgrowth measuring 7 by 6 by 5·5 centimetres. The cut surface was mottled brown and purple, with areas of paler tissue. The left suprarenal gland was located in an abnormal position, being opposite the hilum of the left kidney. Arising from its lower pole there was an ovoid newgrowth of 5 by 4 by 4 centimetres, with appearances similar to those of the tumour on the right side. No evidence of metastases was found. (ii) Cardiac enlargement (heart weight 588 grammes—normal range 270 to 360 grammes) due to left ventricular hypertrophy. (iii) Pulmonary œdema and infarct of the right middle lobe. (iv) Chronic venous congestion of the liver (weight 2300 grammes, normal 1450 to 1700). The kidneys were slightly enlarged and showed striated congestion of the cortical vessels. The brain weighed 1540 grammes (normal range 1370 to 1450 grammes).

Microscopical findings were as follows: (i) The suprarenal tumours show large cells with abundant pale granular cytoplasm. Tumour giant cells are occasionally found. Both lesions are phæochromocytomas. It is generally agreed that criteria of malignancy are unreliable in these growths. (ii) Sections of the kidneys show notable hyalinization of the arterioles, such as is usually found in hypertension. There are no other changes of note. (iii) Sections of the eye show papilloedema. Arterioles similar to those of the kidney are found. (iv) There are unusual changes in sections of the brain. The small vessels in parts of the cortex are very conspicuous. They are frequently ensheathed by spindle cells containing abundant pigment, which gives the staining reactions of melanin. Granules of melanin are also found in isolated cells not associated with these vessels. Similar changes have not been found in a preliminary survey of the literature, and their significance is unknown.

The pathological diagnosis is: (i) bilateral suprarenal phæochromocytomas and congestive heart failure with pulmonary œdema and infarction; (ii) unusual changes in the cortical vessels of the brain with accumulation of melanin pigment.

Discussion.

DR. J. REIMER: Is there any comment regarding the pathological findings?

PROFESSOR F. R. MAGAREY: I am interested in the pigment in the brain, which appears mainly to be in the walls of the small blood vessels and perhaps then broken down to the amino acid tryptophane amongst other things. We know that one of the amino acids essential in the formation of melanin is tryptophane, and perhaps some of the excess tryptophane deposited in the blood vessel walls is converted to melanin.

DR. H. WARDLAW: I think that is highly probable, because adrenaline and nor-adrenaline are converted to substances called adrenochrome, and still further changes lead to the formation of melanin-type pigments.

DR. W. L. CALOV: I would like to ask a question regarding the changes in the arterioles. Would these changes possibly have become necrotizing if they had persisted long enough and the patient had not died before they had time to occur?

DR. A. A. PALMER: I think that, as Dr. Michell has pointed out, necrotizing arteriolitis is related to the degree of the hypertension. If the blood pressure is high, and if it has gone up rapidly, then necrosis occurs. I find it hard to draw a sharp line between arteriolar necrosis and a severe degree of hyalinization. Perhaps Professor Magarey can clear this up.

PROFESSOR F. R. MAGAREY: I agree with you. I think that once the arteriole is hyalinized it is always hyalinized. Occasionally one sees a long-standing benign hypertension that ends up in the malignant phase, and in there one can find both hyalinized vessels and necrotic vessels. But there is nothing to suggest that hyalinized vessels have become necrotic. However, one cannot prove this.

DR. J. REIMER: I would like to call on Dr. Stokes to comment on this case, of which he had some knowledge many years ago in this hospital.

DR. E. H. STOKES: Firstly, I would like very much to congratulate Dr. Michell on the excellent way he presented this case. He is perfectly correct in his diagnosis, and, of course, he could not be expected to guess that there were two tumours. I had charge of this patient many years before phæochromocytoma was widely known and before the diagnosis was as readily made as it is today. At the same time Smithwick was finding unexpected phæochromocytomas in his sympathectomy cases, which indeed this patient had been advised to have.

In this particular instance it is interesting to reflect that had the tumour been found at sympathectomy he would have died earlier than he did, since the tumours were bilateral, little adrenal tissue remained and neither "Regitine" or cortisone was readily available to deal with emergencies. This patient died, of course, from cardiac failure, and the phenomenon of quadruple rhythm is found in the later stages of cardiac failure. In reference to the suggestion of coarctation of the aorta, I suggest that the blood pressure in coarctation is not as high as a rule as it was in this case. I may state that the femoral pulses were palpable during life. With regard to the sweating, I would like to point out that this finding in another patient was followed by exploration, which proved the absence of a chromaffin-cell tumour. The patient died a few days later, and no chromaffin-cell tumour was found. This shows that the sign of sweating is not entirely reliable.

Diagnosis.

Bilateral suprarenal phæochromocytomata, congestive heart failure, pulmonary œdema and infarction.

The World Medical Association.

THE following information has been received from the World Medical Association.

Eleventh General Assembly.

The eleventh General Assembly of the World Medical Association will be held in Istanbul, Turkey, from September 29 to October 5, 1957, in the Conference Hall, Faculty of Science, University of Istanbul.

The theme of the Assembly, celebrating its first decade of activity, will be "Solidarity: The Key to Medical Advancement".

Programme topics will include the following: (i) "The Utilization of the Hospital in Providing Medical Care." Well-qualified speakers, representing medical opinion on this subject from the four representative areas of the world—namely, Asia, Europe, Latin America and North America—will be heard. (ii) "Protection for the Civilian Medical Team in Times of Armed Conflict": (*a*) the provision of universal recognition for a protective emblem; (*b*) the development of a central repository for medical credentials. (iii) "The Interdependence of the Medical and Pharmaceutical Professions", presented by Elmer Severinghaus, M.D., of Hoffman-La Roche (United States of America).

A medical editors' meeting will be held, to discuss (*a*) the role of the medical and lay Press in the health education of the public, and (*b*) integration of medical journals to reduce the number and improve the content. The secretary is Dr. Hugh Clegg, editor of the *British Medical Journal*.

A scientific session will have as its theme "Advancements in Medical Practice in Turkey". Papers will be presented by eminent Turkish leaders of medical science.

The World Medical Association, an international organization of national medical associations, is the only organization at the international level that can speak and represent the opinions of the practising doctors of the world. Its current membership includes 53 national medical associations of the free world, representing more than 700,000 doctors.

Delegations from the majority of the member associations are expected to attend the eleventh General Assembly. In addition, there will be representatives present from numerous international organizations having interests in the field of health, and observers from specialty and component medical societies.

Cuban Doctors Persecuted.

For several months the citizens of Cuba have been "agitating" to "force an election" of national officers. It is alleged that the army and State police have on several occasions wounded individuals taking part in demonstrations. The doctors who have cared for sick and wounded demonstrators have no professional immunity in rendering medical care to these people. In fact, these doctors have been beaten, arrested and imprisoned as political criminals.

In June, the Cuban Medical Association offices were raided during a regular business session. Doctors were taken into custody, and a special edict has been effected making it a criminal offence for the medical association to hold meetings.

Doctors are citizens of their country and must fulfil their duties as citizens. However, the medical doctor is pledged to serve the needs of humanity and pledges himself to permit no consideration of religion, nationality, race, party politics or social standing to intervene between his duty and his patient. Members of the medical and auxiliary professions must be granted the protection needed to carry out their professional activities freely, and the fulfilment of medical duties and responsibilities in no circumstance should be deemed an offence.

The mental and physical health of any nation, regardless of its internal or foreign political situation, depends to a large degree upon the Government recognizing and protecting the doctor in carrying out his humanitarian service.

Medical Practice.

CONDITIONS OF SERVICE FOR FOREIGN DOCTORS IN INDONESIA.

THE following are the general conditions for foreign doctors on a "short-term contract" in the service of the Ministry of Health of the Republic of Indonesia:

1. Foreign doctors (and other workers) can be taken into temporary service of the Government of the Republic of Indonesia on a so-called "short-term contract" of three years. The contract takes effect on the date of the first working day in Indonesia.

2. A medical certificate stating the applicant's fitness for service in the tropics is required.

3. The passage by sea from the country of origin to Indonesia and back for the accepted applicant and his family (wife and children) is paid by the Indonesian Government.

4. For a tropical outfit an allowance of f. 1000 (Netherlands guilders) or the equivalent in the currency of the country of origin is paid. For the family (*in toto*) 50% extra is paid.

5. Salary in Indonesia.[1] The monthly basic salary in Indonesia for doctors (and other university graduates) who have just finished their study will amount to Rp. 450 (Indonesian currency). For those with two years' continuous practice after graduation it will amount to Rp. 540. Further rates are: four years after graduation, Rp. 610; six years after graduation, Rp. 720; eight years after graduation, Rp. 790; ten years after graduation, Rp. 860; thirteen years after graduation, Rp. 930; sixteen years after graduation, Rp. 1000; nineteen years after graduation, Rp. 1075. Special allowances are paid in addition to the basic salary, viz.: (*a*) a cost-of-living allowance (+50% if married; +25% if single); (*b*) a children allowance (+10% for each child); (*c*) an allowance of Rp. 300 a month as a compensation for the lack of income from private practice for general practitioners, and Rp. 400 for specialists; (*d*) an extra "foreigners-allowance" (25% of the net income taxes deducted); (*e*) for doctors with five or more years' continuous practice after graduation a special allowance of 20% of the monthly basic salary is paid in the country of origin at a rate of exchange of 1 Rp. = 1 Netherlands guilder. In this case the "bonus" of one month basic salary for every year of service will be cancelled.

6. If the family (wife and children) is staying in the country of origin, it is allowed to transfer monthly a certain amount for alimentation purposes. This amount depends on the monthly income.

7. After expiration of the contract an extra amount of 25% of the basic monthly salary for every month of service *plus* one month's basic salary for every year of service will be paid out in the currency of the country of origin at a rate of exchange of 1 Rp. = 1 Netherlands guilder.

8. Provisional salary. From the date on which the Indonesian Government notifies him that he must be prepared for departure until the arrival in Indonesia the accepted applicant will receive a provisional salary of +40% of the basic salary.

9. Service on a "short-term contract" gives the status of government official temporary service. Consequently all government personnel regulations (for example, the regulations concerning restitution of a part of the expenses for medical treatment, sick leave, holidays, and so on) are applicable to these officials.

10. From an applicant the following documents are required: (*a*) Personal history: (i) name, (ii) date and place of birth, (iii) nationality, (iv) sex, (v) marital status (single, married, divorced, widowed), (vi) children (number, age and sex, school), (vii) knowledge of languages. (*b*) Authorized copies of certificates of qualification. (*c*) Exact statement of the hospitals and institutes where the applicant has worked. (*d*) Some references. (*e*) Remarks, if any.

11. If an applicant is accepted, the necessary formalities (signing of the contract, the arrangement of the trip to Indonesia, *etc.*) will be carried out: (*a*) For all European countries by the "Committee for Recruitment of Foreign Experts to Indonesia", Stadhouderslaan 128 s-Gravenhage. (*b*) For other countries by the Indonesian embassy or legation in that country. The Indonesian embassy in Australia is at Canberra.

[1] £1 (Australian) = 25 Rupiahs (Rp.). The following figures indicate the cost of essential items in Indonesia: one kilogram of beef = Rp 16,–; one kilogram of potatoes = Rp. 3,–; one kilogram of sugar = Rp. 3,40; one kilogram of rice = Rp. 2,50; one kilogram of coffee = Rp 20,–; one chicken = Rp. 20,–; one egg = Rp. 0,80; one loaf of bread = Rp. 2,50; one pound of tea = Rp. 3,–; one tin of margarine (five pounds) = Rp. 17,50; one kilogram of fish = Rp. 17,50; one three-bedroom house = Rp. 100,– per month; one servant = Rp. 100,– per month.

THE USE OF ANTIBIOTICS.

THE Antibiotics Committee of the National Health and Medical Research Council has drawn up a table indicating the use of antibiotics in various diseases. It is published herewith at the request of the Director-General of Health, Commonwealth Department of Health, Canberra. Under the headings of the several antibiotic preparations the numbers 1, 2 and 3 refer to the preferences in order in which the drugs should be used, in other words which drug would be expected to provide most benefit in a particular illness.

Notes.

1. Whenever possible, sensitivity tests should be carried out and the appropriate antibiotic used. This is particularly important in staphylococcal infections.

2. *Staphylococcal Infections.*—The choice of antibiotics for the treatment of staphylococcal infections has become increasingly difficult because of the greater number of strains of the organism which are antibiotic-resistant. There are many cases in which this organism has been resistant to all antibiotics. The problem is further aggravated because the organism is widespread and causes many types of infections, ranging from skin lesions to generalized

Number.	Disease.	Sulphonamides.	Penicillin.	Chlortetracycline ("Aureomycin").	Oxytetracycline ("Terramycin").	Tetracycline ("Achromycin" or "Tetracyn").	Chloramphenicol ("Chloromycetin").	Streptomycin.	Erythromycin.	Remarks.
1	Hæmolytic streptococcus (group A) infections.	—	1	2	2	2	—	—	3	Resistance to antibiotics not a problem. Use penicillin first. Most cases will respond.
2	*Streptococcus viridans* (endocarditis) infections.	—	1	3	3	3	—	1	2	Combined therapy: penicillin in large doses *plus* streptomycin in doses of two grammes per day up to a total of 20 grammes (adult).
3	*Streptococcus fæcalis* (endocarditis) infections.	—	1	2	2	2	—	1	2	Combined therapy as for number 2.
4	Puerperal infections ..	See remarks	1	2	2	2	—	—	3	Combined penicillin and sulphonamide therapy will control over 90% of all obstetrical infections. The others except staphylococcal infections will usually respond to one of the tetracyclines. The remarks concerning staphylococcal infections are given below under 9. Full details of treatment of puerperal mastitis are set out in N.H.M.R.C. Special Report, Series No. 7 (1956), "Staphylococcal Infections in Maternity Hospitals".
5	Anaerobic streptococcal infections.	See remarks	1	2	2	2	—	—	3	
6	Pneumococcal infections ..	—	1	2	2	2	3	—	2	Resistance to antibiotics not a problem. Should respond to penicillin.
7	Meningococcal infections ..	1	1	2	3	2	3	—	2	Combined antibiotic and sulphonamide therapy.
8	Gonococcal infections ..	1	1	2	2	2	3	—	2	
9	Staphylococcal infections: ..	—	—	—	—	—	—	—	—	See notes under heading "Staphylococcal Infections".
	(*a*) In hospitals	—	—	—	—	—	—	—	—	
	(*b*) In general practice ..	—	—	—	—	—	—	—	—	
10	Brucellosis	See remarks	—	2	2	2	1	2	—	Combined antibiotic and sulphonamide therapy gives best results.
11	Pertussis	—	—	2	1	2	2	—	3	
12	Typhoid fever	—	—	2	2	2	1	—	—	
13	Influenzal meningitis ..	See remarks	—	2	—	2	1	1	—	Combined antibiotic and sulphonamide therapy with *Hæmophilus influenzæ* antiserum.
14	Urinary tract infections (uncomplicated):									The occurrence of antibiotic-resistant strains of the Gram-negative bacilli is a problem in this group, the development of resistance following no special pattern. Sensitivity tests should be done. In general practice various antibiotics may have to be tried. Combinations may be found useful. Sulphonamides should be tried first. See notes (6) and (7) below on polymyxin and bacitracin. Nitrofurantoin, which is marketed as "Furadantin", and which is a synthetic antibacterial agent, may be used in Gram-negative bacillary infections if the organisms are resistant to antibiotics but sensitive to "Furadantin".
	(*a*) *Escherichia coli* ..	See remarks	—	1	1	1	2	2	—	
	(*b*) *Bacillus aerogenes* ..	See remarks	—	1	1	1	2	2	—	
	(*c*) *Proteus vulgaris* ..	See remarks	—	2	—	2	1	1	—	
	(*d*) *Pseudomonas pyocyanea*	See remarks	—	2	1	1	—	1	—	
	(*e*) *Streptococcus fæcalis* ..	See remarks	2	1	1	1	1	3	2	
15	Tuberculosis	—	—	—	—	—	—	1	—	Streptomycin should never be given alone. It is felt that in the first instance, except in acute cases, isoniazid and PAS should be given and streptomycin kept in reserve. In acute cases streptomycin, isoniazid and PAS should be given together. The preferred dose of streptomycin is one gramme twice weekly, except in acute cases, when one or two grammes daily may be given for a short period. See note (9) below in regard to viomycin.
16	Chancroid	—	—	1	—	2	—	—	—	
17	Friedländer bacillus (pneumonia).	—	—	1	1	1	2	1	—	
18	Salmonella infections (gastroenteritis and bacteriæmia).	—	—	2	2	2	1	1	—	
19	Bacillary dysentery	1	—	2	2	2	2	2	—	
20	Plague	1	—	—	—	—	—	1	—	
21	Subacute bacterial endocarditis:									
	(*a*) *Streptococcus viridans* (see above).	—	1	3	3	3	—	1	2	Combined penicillin and streptomycin.
	(*b*) *Streptococcus fæcalis* ..	—	1	2	2	2	—	1	2	Combined penicillin and streptomycin.
	(*c*) *Hæmophilus influenzæ*	See remarks	—	2	—	2	1	1	—	Combined antibiotic and sulphonamide therapy.
22	Acute bacterial endocarditis:									
	(*a*) Staphylococcal ..	—	—	—	—	—	—	—	—	As above under number 7.
	(*b*) Other organisms ..	—	—	—	—	—	—	—	—	As above for corresponding organism.
23	Trachoma	1	—	2	—	2	—	—	—	
24	Surgical conditions of bowel (pre- and post-operative).	1	—	—	—	—	1	1	—	Combined antibiotic and sulphonamide therapy.
25	Pulmonary conditions (pre- and post-operative).	—	1	1	1	1	2	2	3	Depends on organism causing infection.
26	Typhus and other rickettsial diseases.	—	—	2	2	2	1	—	—	
27	Primary atypical pneumonia	—	—	1	1	1	—	—	—	The antibiotics have no effect on the primary disease but do control the secondary infection.
28	Psittacosis	—	—	1	2	1	—	—	—	
29	*Lymphogranuloma venereum* ..	—	2	1	1	1	3	—	—	Antimony preparations may also be used.
30	*Granuloma inguinale*	—	2	1	1	1	3	—	—	
31	Anthrax	—	1	2	2	2	—	—	—	Combined with antiserum.
32	Syphilis	—	1	2	2	2	—	—	—	
33	Yaws	—	1	2	2	2	—	—	—	Arsenical compounds may also be given.
34	Rat-bite fever:									
	(*a*) *Spirillum minus* ..	—	2	1	—	1	—	—	—	
	(*b*) *Streptobacillus moniliformis*.	—	—	—	—	—	—	1	—	
35	Tularæmia	—	—	1	1	1	—	1	—	
36	Gas gangrene	—	1	2	2	2	—	—	—	Combined with antiserum.
37	Influenza	—	—	—	—	—	—	—	—	
38	Common cold	—	—	—	—	—	—	—	—	Virus diseases do not respond to any antibiotic, rickettsial diseases do.

Number.	Disease.	Sulphonamides.	Penicillin.	Chlortetracycline ("Aureomycin").	Oxytetracycline ("Terramycin").	Tetracycline ("Achromycin" or "Tetracyn").	Chloramphenicol ("Chloromycetin").	Streptomycin.	Erythromycin.	Remarks.
39	Infectious mononucleosis ..	—	—	—	—	—	—	—	—	
40	Infective hepatitis and homologous serum hepatitis.	—	—	—	—	—	—	—	—	
41	Actinomycosis	See remarks	1	2	2	2	—	—	—	Penicillin should be given in large doses and may be combined with sulphadiazine. Tetracycline can be alternated with penicillin.
42	Amœbiasis	—	—	1	1	1	—	—	—	Emetine or satisfactory substitutes should be used with the antibiotics.
43	Leptospirosis (Weil's disease)	—	1	2	—	2	—	—	—	
44	Diphtheria (see remarks) ..	—	1	2	2	2	—	—	—	Antiserum essential.
45	*Herpes zoster*	—	—	1	—	1	2	—	—	
46	Tetanus (see remarks) ..	—	1	2	2	2	—	—	—	Antiserum essential.
47	Fungal infections	—	—	—	—	—	—	—	—	Mycostatin may be effective in lesions due to *Candida albicans* (monilia). It can be used locally or taken by mouth according to the site of the infection.

systemic infections. At first the problem of antibiotic-resistant strains was mainly a problem of hospitals. Today it is also a problem of general practice. Investigations would indicate that, apart from furunculosis, patients, either adult or children, who have acquired a staphylococcal infection by cross-infection in hospital have a 75% chance that the organism will be penicillin-resistant, a 27% chance that it will be streptomycin-resistant and a 6% chance that it will be resistant to all antibiotics. If the patient has a staphylococcal infection and is being treated in the casualty department of a hospital, there is a 50% chance that the organism will be penicillin-resistant. If the patient is being treated in private practice and has had no contact with a hospital, there is a 25% chance that the organism will be penicillin-resistant. In all patients suffering from boils, either in private practice or in a hospital, there is a 60% to 65% chance that the staphylococcus will be penicillin-resistant. It is alarming to note that 25·7% of nasal carriers of *Staphylococcus aureus* in the general population carry penicillin-resistant strains. This is twice the number found two years ago. In staphylococcal infections it is essential that sensitivity tests be carried out as soon as possible and that they be repeated during therapy if the organism can still be grown in culture. What is to be the choice of antibiotics while the result of the sensitivity test is being awaited? It is certain that penicillin should not be the first choice if the patient has been cross-infected in hospital or is suffering from boils. It is doubtful whether penicillin should be the first choice in private practice because of the 25% chance of the organism being penicillin-resistant. It would probably be wise to use an antibiotic other than penicillin for forty-eight hours until the results of the sensitivity tests are known. When sensitivity tests are quite unavailable, it would seem that in severe staphylococcal infections antibiotics other than penicillin should be used; in mild infections it may be permissible to try penicillin in the first instance, but to change to some other antibiotic if there is no clinical response in thirty-six hours. There is abundant evidence to indicate that the staphylococcus develops resistance to chloramphenicol more slowly than to other antibiotics, and except in severe staphylococcal infections this antibiotic should be held in reserve until other antibiotics have been tried. It should be pointed out that chloramphenicol-resistant strains of the organisms are increasing in number. It should also be remembered that chloramphenicol may have a depressant effect on the hæmopoietic system. Erythromycin (marketed as "Ilotycin" and "Erythrocin") is effective against *Staphylococcus aureus*, but there is evidence that resistance can develop in as short a time as thirty-six hours. The new antibiotic novobiocin, which is marketed under various names such as "Albamycin", "Cathomycin", "Cardelmycin" *etc.*, is effective against various Gram-positive organisms, especially staphylococci. Novobiocin is exceedingly toxic, the manifestations usually arising within seven days. When erythromycin first became available, its use was restricted, so that it would be used only when the organism had become resistant to all other antibiotics. It is felt that the use of novobiocin should be restricted in the same way, as this will prolong the period of maximum value of this new antibiotic and should delay the appearance of resistant strains of organisms. These remarks should also apply to rovomycin. In summary, it is suggested that in choosing an antibiotic for staphylococcal infections, the following plan might be followed: (i) A culture be made and sensitivity tests carried out. (ii) One of the tetracyclines be used in the first instance preceding the results of the sensitivity test. (iii) When the results of the sensitivity tests are known, (*a*) a change should be made to penicillin if the organism is penicillin-sensitive, (*b*) tetracyclines should be continued if the organism is not sensitive to penicillin but sensitive to tetracycline, (*c*) if the organism is penicillin-resistant and tetracycline-resistant, the other antibiotics to which the organism is sensitive should be used, the following order of preference being suggested—erythromycin, chloramphenicol, novobiocin, (*d*) streptomycin in doses of 0·5 gramme twice a day up to a total dose of 20 grammes may be used, if the organism is sensitive; it may be combined with any of the other antibiotics. Nasal carriers of *Staphylococcus aureus* may be treated by the local application of neomycin and bacitracin to the nasal cavity twice a day for one week. The course may be repeated if further cultures are still positive.

3. Penicillin V (phenoxymethyl penicillin) is a new preparation for oral penicillin therapy. Penicillin V resists the action of the acid secretions of the stomach, and on the evidence available it is better absorbed than is penicillin G. If a single dose of 200,000 units of penicillin V is given orally, the resultant blood level of penicillin is comparable with that obtained by a single intramuscular injection of penicillin G. If the single dose is above 200,000 units, it is thought that higher blood levels are obtained from intramuscular injections. Penicillin V given orally does not replace injectable penicillin in the treatment of severe infections. A penicillin V tablet of 60 milligrammes is equivalent to 100,000 units of penicillin G.

4. While combinations of some antibiotics are often useful, as indicated in the worksheet, penicillin, which is bactericidal, should not be given with the tetracyclines or chloramphenicol, as these antibiotics tend to interfere with the action of penicillin.

5. Polymyxin has not been included in the worksheet, as it is a highly toxic antibiotic and should be used only under careful supervision with the patient in hospital. Polymyxin is effective against some strains of *Pseudomonas pyocyanea*.

6. Bacitracin is not included in the worksheet, as the product at present available is suitable for local application only.

7. Neomycin, because of its toxicity, has not been included. However, its usefulness for topical application in some conditions is recognized.

8. It is considered that viomycin in the recommended dose of two grammes twice per week is a safe antibiotic, as complications are relatively rare, but it should be reserved for hospital and/or sanatorium treatment.

9. Attention is drawn to the National Health and Medical Research Council Special Report Series No. 6, 1955, "Chemotherapy with Antibiotics and Allied Drugs", and No. 7, 1956, "Staphylococcal Infections in Maternity Hospitals".

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

THE SOUDAN CONTINGENT.[1]

[From *The Australasian Medical Gazette*, March, 1885.]

THE Ambulance Corps which accompanied the New South Wales Contingent of troops for the Soudan consists of Surgeon-Major Dr. W. D. C. Williams (of Darlinghurst, Sydney) in command, Surgeon Dr. Doyle Glanville (late surgeon of P. and O. R.M.S. "Rome") and Surgeon Dr. George Proudfoot (late of Byerock). Also two non-commissioned officers and two dispensers together with 24 trained bearers many of whom are men of long service in army hospital corps, five drivers and one trumpeter. There are five ambulance waggons, fully fitted up on latest Service principles, each waggon to carry seven wounded—two on front seat, two inside on stretchers which have been so arranged that when in position but very little motion will be felt, and three on the back seat. There are also two pharmacy and surgical waggons, fitted with instruments, drugs, medical comforts and medical panniers, in such a way that each article is placed in boxes and drawers which are lettered and numbered so that the articles can be at once procured. Two waggons will be provided for carrying tents both hospital and operating: bedding clothes and reserve stores: two field waggons fitted up to carry general hospital stores: one water cart.

Correspondence.

VENOUS RETURN.

SIR: Through the courtesy of my publisher, Grune and Stratton, Inc., New York, I received a clipping of the review of my book, "Venous Return", which appeared in THE MEDICAL JOURNAL OF AUSTRALIA, March 2, 1957.

I note that the reviewer has mis-stated an important point. This concerns the purpose of the book. The reviewer writes: "'Venous Return', by Gerhard A. Brecher, is described both by Wiggers in the foreword and by the author in his preface as a comprehensive analysis of venous return to the heart." The reviewer then proceeds with two statements by which he infers that this is a false or exaggerated claim of the author. The reviewer then writes: "It presents the results of surveying some of the literature, especially the more recent American literature, and of the author's own experiments. . . . Neglect of much literature is not compensated for by the author's own clarity of thought."

I have neither inferred nor claimed that my monograph is "a comprehensive analysis of venous return to the heart". I have clearly stated and emphasized that this is not the case by calling the reader's attention to the limits of the book. For documentation I quote from the preface: "A treatise on the subject appears desirable because no comprehensive work on the venous system has been published since Kenneth J. Franklin's 'A Monograph on Veins' in 1937. The present book is not intended to survey the entire field of venous physiology and anatomy since 1937 as Franklin's monograph does up to that date. Its scope is more limited. It will deal specifically with the dynamic aspects of the return flow of blood to the heart." "In addition to Franklin's book, I wish to refer to other accounts of certain aspects of the venous system, whose contents I have not intended to duplicate. The reader should consult them for information on the specific problems treated there. The basic principles of correlation in the circulatory system are enunciated in the article (*'Venensystem und Kreislaufregulierung'*) (1932) by the late Klothilde Gollwitzer-Meier. A detailed study of venous flow dynamics with the aid of X-ray cinematography is reported by W. Böhme in the account *'Über den aktiven Anteil des Herzens an der Förderung des Venenblutes'* (1936). Landis and Hortenstine have emphasized the inter-relation of venous pressures and fluid exchange in their review on 'Functional Significance of Venous Pressure' (1950). Two books of G. E. Burch, 'A Primer of Venous Pressure' (1950) and 'Digital Plethysmography' (1954), deal with the methods and clinical applications of venous pressure measurements and of plethysmographic flow recordings respectively."

Almost the entire older world literature on the subject is available in the books and articles quoted in "Venous Return". This refers also to Conheim, who is singled out by the reviewer as an example for lack of bibliographical completeness. Space and price limit of a monograph do not permit extensive requotations.

If the writer of the book's foreword, Dr. Carl J. Wiggers, expresses an opinion as to the comprehensiveness of the work, it is not up to the author to take issue with him. However, Dr. Wiggers has clearly qualified the limits of comprehensiveness by stating: "The present monograph not only presents a comprehensible, comprehensive account of Dr. Brecher's contributions, but also an excellent historical survey of work preceding his own studies." "This monograph is the only current one that gives a comprehensive analysis of the determinants of venous return and its adaptation to cardiac output based on experimental measurement of venous flow."

Based on the above quotations, it becomes evident that the reviewer does not inform the reader properly as to the scope of the monograph. I am therefore doubtful if the review conveys an appraisal which the reader can place reliance into.

Yours, etc.,

GERHARD A. BRECHER, M.D., Ph.D.

Department of Physiology,
The Ohio State University,
Columbus 10,
United States of America.
May 13, 1957.

[The reviewer comments as follows:

Thank you for referring to me Dr. Brecher's comments on my review of his book "Venous Return". In my review I stated that the claim for comprehensiveness applied to venous return to the heart. This is definitely stated in the foreword, and I think the author must take responsibility for what is stated in the foreword—he accepts it and publishes it. After careful re-reading of the book, I still think the author implies comprehensiveness in relation to venous return to the heart. In the quotation in the third paragraph of Dr. Brecher's letter, he states that Franklin has dealt with the entire field of venous physiology and anatomy comprehensively, but that the present author will deal with "the return flow of blood to the heart". Then in Chaper I, "Historical Considerations", the author goes back as far as "Aristotle (384-322 B.C.)" on this subject. I got the impression that the claim was for comprehensive historical and experimental analysis of the matter of venous return to the heart.

My main criticism, however, was concerned with basic theoretical considerations. Controversy over what the author meant to say about the comprehensiveness of his book is not cogent argument against my criticisms of his hydrodynamical concepts. If he cares to enter into controversy on these I will be ready to defend my statements or admit error.]

FEDERATION OF COUNTRY LOCAL ASSOCIATIONS SIXTH POST-GRADUATE COURSE.

SIR: Would you please permit me, through your columns, to bring to the notice of your readers that the sixth post-graduate course under the auspices of the Federation of Country Local Associations will be held this year in Maitland, New South Wales, from September 16 to 20.

The men who have kindly consented to lecture are all eminent in their particular field, and their subjects cover a very wide range of the work of the general practitioners.

An attractive and interesting social side has been arranged, and special consideration has been given to the entertainment of members' wives.

The fee for the course is twelve guineas, or three guineas per day.

Full details may be had on application to me.

Yours, etc.,

R. H. K. McKERIHAN,
Course Secretary.

35 High Street,
East Maitland,
July 12, 1957.

[1] From the original in the Mitchell Library, Sydney.

Post-Graduate Work.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

PROGRAMME OF POST-GRADUATE COURSES, AUGUST TO DECEMBER, 1957.

THE Post-Graduate Committee in Medicine in the University of Sydney announces the following programme for the period from August to December, 1957.

Week-End and Metropolitan Courses.

Pædiatrics.—A week-end course in pædiatrics will be held on August 3 and 4 at the Royal Alexandra Hospital for Children, full time. The fee, including luncheons, is £4 16s.

Reunion Week, Royal North Shore Hospital.—Reunion week at the Royal North Shore Hospital will be held from August 12 to 17. Mr. A. Dickson Wright, surgeon to St. Mary's Hospital and the Prince of Wales Hospital, London, will be guest speaker, and a limited number of vacancies has been reserved for non-members to attend this full-time course on enrolment through the Post-Graduate Committee. The fee is £5 5s.

Obstetrics and Gynæcology.—A course in obstetrics and gynæcology will be conducted by the staff of the Women's Hospital, Crown Street, full time, at which Professor R. J. Kellar, Professor of Obstetrics and Gynæcology in the University of Edinburgh, will be guest speaker. Enrolments are limited to 14 students in residence and 12 attending as external students. The fees are £8 18s. 6d. (including board and residence) or £6 6s. (external attendance).

Refresher Week, Sydney Hospital.—Refresher week at Sydney Hospital will be held from September 9 to 13. Professor J. G. Hayden, of Melbourne, will be guest speaker, and a limited number of vacancies has been reserved for non-members to attend this full-time course on enrolment through the Post-Graduate Committee. The fee is £5 5s.

Reunion Week, Royal Prince Alfred Hospital.—Reunion week at Royal Prince Alfred Hospital will be held from September 13 to 20. Professor C. A. Wells, Professor of Surgery in the University of Liverpool and McIlrath Guest Professor to the Royal Prince Alfred Hospital, will be guest speaker. A limited number of vacancies has been reserved for non-members to attend this full-time course on enrolment through the Post-Graduate Committee. The fee is £5 5s.

Rheumatic Diseases.—A week-end course in rheumatic diseases will be held at the Royal Prince Alfred Hospital on October 12 and 13. The fee is £3 3s.

Dermatology.—Two week-end courses in dermatology will be held in Sydney on November 9 and 10 and on November 16 and 17, further details of which will be announced shortly. The fee is £3 3s. for each week-end.

Hæmatology.—A week-end course in hæmatology will be held on November 16 and 17 at the New Medical School, University of Sydney, full time. The fee is £4 4s.

Psychosomatic Medicine.—A week-end course in psychosomatic medicine will be held in Sydney on November 23 and 24, details of which will be published shortly.

Occupational Medicine.—A week-end course in occupational medicine will be held at the Royal Prince Alfred Hospital and at the School of Public Health and Tropical Medicine on November 30 and December 1. The fee is £3 3s.

Mental Deficiency.—A week-end course in mental deficiency will be held on November 30 and December 1 at the Mental Hospital, Newcastle, for a limited number of selected candidates. Details of the programme and the fee for attendance will be announced shortly.

Course in Surgery.—A part-time course in surgery will be held in Sydney early in December, details of which will be announced later. The course has been designed to coincide with the visits of Mr. Owen H. Wangensteen, Professor of Surgery in the University of Minnesota, and Director of the Department of Surgery, University Hospital, Minnesota, and Mr. Robert H. Linton, Associate Surgeon to the Massachusetts General Hospital, Boston, and Assistant Clinical Professor of Surgery, Harvard Medical School. It is expected that the following lectures will be given by Mr. Wangensteen: "Intestinal Obstruction", "Is There a Place in Surgery for the Management of Coronary Artery Disease?", "Œsophagitis", "Hiatus Hernia and Cardiospasm", "Extended Operation for Alimentary Tract Cancer" and "The Second Look", "Biliary Tract Surgery", "Experimental and Clinical Studies of Peptic Ulcer", "Cancer Detection". Mr. Linton is expected to speak on "Portal Hypertension", "Thrombo-embolism" and "Varicose Veins and Varicose Ulcers". This course will be available to members of the annual subscription course without charge.

Annual Subscription Course: Alteration to Programme.

Mr. A. Dickson Wright will lecture on "Ulcerative Colitis" at the Royal Prince Alfred Hospital on Thursday, August 8, at 8.15 p.m., instead of the date previously announced.

Diploma Courses.

Part I courses for the D.A., D.G.O., D.L.O. and D.O. of the University of Sydney will be held in Sydney from September 2 to November 15. The fee for attendance at each course is 35 guineas.

Part II courses for the D.G.O., D.L.O. and D.O. will begin on November 25, 1957, and continue until March, 1958.

Post-Graduate Country Conferences.

Country conferences will be held as follows: Newcastle: August 17 and 18, medicine, and November 23 and 24, surgery. Albury: August 31 and September 1. Coff's Harbour: September 14 and 15. Parramatta: October 19 and 20. Bega: November 16 and 17.

Clinical Meetings at Balmoral Naval Hospital.

The following meetings will be held at the Balmoral Naval Hospital from August to December, beginning at 2 p.m.: Tuesday, August 13: "Common Skin Diseases and Their Treatment", Dr. A. Geoffrey Finley. Tuesday, September 10: "Recent Advances Abroad", Dr. K. J. Fagan. Tuesday, October 8: "Impressions of Medical Advances Overseas", Dr. Selwyn Nelson. Tuesday, November 19: "Treatment of Eye Conditions Encountered in Service Personnel", Dr. E. W. Freshney. Tuesday, December 10: "Psychosomatic Diseases", Dr. T. M. Greenaway. All members of the medical profession and senior medical students are invited to attend these meetings.

Post-Graduate Residencies.

Anæsthesia.—Post-graduate residencies in anæsthesia, each of five days' duration, are now available at the Royal Newcastle Hospital for 1958. The fee (including board and residence) is £5 15s. 6d. No reservations can now be made for 1957.

General, for Women Medical Graduates.—Post-graduate residencies for women medical graduates are available at the Rachel Forster Hospital for Women and Children, Redfern, for periods from one to two weeks or longer by arrangement. Intending applicants should state the period of resident training required and any special interests. The fee (including board and residence) is £6 6s. per week.

Obstetrics and Gynæcology.—Post-graduate residencies for one or more weeks are available at The Women's Hospital, Crown Street, and at the Royal Hospital for Women, Paddington. The fee (including board and residence) is £5 15s. 6d. per week.

General Revision Course, 1958.

The annual general revision course will be conducted in Sydney for two weeks from May 5 to 16, 1958. The main theme of the course will be therapeutics, and in addition the programme will, as in former years, be a comprehensive survey of modern trends in diagnosis and treatment of special value to general practitioners. The fees for attendance are £12 12s. (full time) or £6 6s. (part time or one week only).

Taxation Deductions.

A deduction may be claimed in respect of fees paid for attendance at courses held under the Committee's auspices, when such fees are paid by medical practitioners who are in practice. Travelling expenses incurred in attending such courses may also be claimed as a deduction. When deductions are claimed, it is necessary to quote "Taxation File No. AF/1865".

Method of Enrolment and General Information.

In all cases, application for enrolment in post-graduate courses should be made to the Course Secretary, The Post-Graduate Committee in Medicine, 131 Macquarie Street, Sydney. All fees are payable in advance. Telephones: BU 4497-8. Telegraphic address: "Postgrad Sydney."

NUFFIELD FOUNDATION DOMINION TRAVELLING FELLOWSHIPS.

For Australian Graduates.

THE Nuffield Foundation will continue in 1958 its scheme of offering a number of Travelling Fellowships to Australian graduates. Seven awards will be available, including two fellowships in medicine, two fellowships in the natural sciences and two fellowships in the humanities and social sciences.

The purpose of the fellowships is to enable Australian graduates of outstanding ability to gain experience and training in the United Kingdom in their chosen fields, and to make contact there with scholars working in those fields, with a view to the Fellows' equipping themselves to take up posts in teaching or research, or both, in Australia.

The fellowships are intended for men or women of first-rate intellectual and personal qualities, who have already shown unusual capacity to advance knowledge and teaching in one of the fields concerned. The Foundation wishes the awards to be open on as wide a basis as possible, and applications from persons with degrees in such fields as dentistry, veterinary science, engineering, architecture, *etc.*, as well as those in the fields already mentioned, will be welcome. Candidates must be Australian nationals, normally between the ages of twenty-five and thirty-five years, and must be university graduates holding, preferably, a master's or doctor's degree, and having subsequently had a year or more of teaching or research experience on the staff of a university or comparable institution.

A fellowship will normally be tenable for one year, but in exceptional cases may be extended for a further period of a few months. The fellowship will provide for return travelling expenses, at tourist rates, of a Fellow between his home residence and the United Kingdom and, if he is married, similar expenses for his wife; an adequate allowance will be made for the Fellow's living and travelling expenses in the United Kingdom and for his academic fees, books and other incidental expenses, as well as a personal allowance. The total value of an award, including all travelling expenses, varies with the needs and family responsibilities of the holder, but will in no case be less than £900 sterling.

A Fellow will be expected to resume residence in Australia on the completion of the fellowship.

Except with the express permission of the trustees of the Foundation, a Fellow may not hold any other award concurrently with the fellowship.

A Fellow will be required to carry out, at centres approved by the trustees of the Foundation, a programme of research work and training, similarly approved. Other work, paid or unpaid, may not be undertaken without the permission of the trustees. During the tenure of the fellowship, a Fellow will not normally be permitted to prepare specifically for, or to take, examinations for higher degrees or diplomas awarded by bodies in the United Kingdom.

A Fellow will be required to submit to the trustees, at the end of the fellowship, a report on his work during the period of the fellowship.

Should the trustees at any time find that a Fellow neglects or has neglected the obligations of the appointment, they shall have power immediately to terminate the fellowship.

The fellowships will be awarded by the trustees of the Foundation on the recommendation of its Advisory Committee in Australia.

Applications for fellowships to begin in 1958 should be submitted not later than September 12, 1957, to The Secretary, The Nuffield Foundation Australian Advisory Committee, University of Melbourne, Carlton, N.3, Victoria, from whom copies of the application form may be obtained. Applications must be accompanied by a programme of intended work in the United Kingdom in as specific terms as possible.

Naval, Military and Air Force.

APPOINTMENTS.

THE following appointments, changes *et cetera* have been promulgated in the *Commonwealth of Australia Gazette*, No. 34, of June 13, 1957.

NAVAL FORCES OF THE COMMONWEALTH.

Citizen Naval Forces of the Commonwealth.

Royal Australian Naval Reserve.

Appointment.—Dennis Alexander Bloomfield is appointed Surgeon Lieutenant, dated 20th March, 1957.

Promotions.—Surgeon Lieutenant Rex Justice John Gray is promoted to the rank of Surgeon Lieutenant-Commander, dated 2nd May, 1957. Surgeon Lieutenant John Damien Tange is promoted to the rank of Surgeon Lieutenant-Commander, dated 12th February, 1957.

Royal Australian Naval Volunteer Reserve.

Appointment.—Surgeon Lieutenant Francis Victor Harder, Royal Australian Naval Reserve, is appointed Surgeon Lieutenant, with seniority in rank of 13th August, 1952, dated 8th March, 1957.

Resignation.—The resignation of Collins Louis Greaves of his appointment as Surgeon Lieutenant is accepted, dated 5th December, 1956.

AUSTRALIAN MILITARY FORCES.

Royal Australian Army Medical Corps (Medical).

3/40141 Captain H. A. Poulier is transferred to the Reserve of Officers (Royal Australian Army Medical Corps (Medical)) (Southern Command), 18th April, 1957.

To be Major (provisionally), 24th December, 1956: 3/40109 Captain (Temporary Major) A. O. Donald.

Major-General F. Kingsley Norris, C.B., C.B.E., D.S.O., E.D., Retired List, is appointed an Honorary Colonel of the Royal Australian Army Medical Corps, 6th May, 1957.

Major-General Sir Samuel Burston, K.B.E., C.B., D.S.O., V.D., Retired List, relinquishes the appointment of Honorary Colonel of the Royal Australian Army Medical Corps, 5th May, 1957.

Citizen Military Forces.

Northern Command.

Royal Australian Army Medical Corps (Medical).—1/62657 Captain R. A. Rimington is appointed from the Reserve of Officers, 12th April, 1957. 2/104175 Captain N. R. Scott-Young is transferred to the Reserve of Officers (Royal Australian Army Medical Corps (Medical)) (Northern Command), 5th April, 1957.

Eastern Command.

Royal Australian Army Medical Corps (Medical).—2/206953 Major T. M. Greenaway relinquishes the temporary rank of Lieutenant-Colonel, 1st June, 1957, and is placed upon the Retired List (Eastern Command) with permission to wear the prescribed uniform, 2nd June, 1957. To be Captain (provisionally), 1st May, 1957: 2/122031 Harold William Thurlow.

Southern Command.

Royal Australian Army Medical Corps (Medical).—The age for retirement of 3/50203 Colonel E. S. J. King is extended until 10th June, 1959.

3/101809 Captain (provisionally) J. K. Clarebrough ceases to be seconded whilst undergoing post-graduate studies in the United Kingdom, and relinquishes the provisional rank of Captain, 27th March, 1957, is transferred to the Reserve of Officers (Royal Australian Army Medical Corps (Medical)) (Southern Command), and is granted the honorary rank of Captain, 28th March, 1957. To be Majors, 2nd May, 1957: Captains 3/129041 B. C. A. Stafford and 3/101828 H. A. Jenkins, and 3/50211 Captain (Temporary Major) P. Kaye.

Reserve Citizen Military Forces.

Royal Australian Army Medical Corps (Medical).

Northern Command.—To be Honorary Captain, 23rd April, 1957: Kenneth John Carroll.

Eastern Command.—To be Honorary Captain, 1st May, 1957: Noel Arnold Renouf.

ROYAL AUSTRALIAN AIR FORCE.

Permanent Air Force.

Medical Branch.

The following are appointed to a short-service commission, on probation for a period of twelve months, with the rank of Flight Lieutenant: William Iain Stuart (0310760), 15th

March, 1957; Geoffrey Carlyle Nelson (018487), 1st April, 1957; George Duncan (0310761), 25th April, 1957.

Herbert Thomas Cutler (0314200) is appointed to a temporary commission, 1st January, 1957, with the rank of Pilot Officer (Student).

The probationary appointment of the following Flight Lieutenants is confirmed: C. F. Campbell (014785), G. C. Fisk (0310757).

Pilot Officer (Student) I. L. Ferguson (0312882) is granted twelve months' special leave without pay, 29th October, 1956.

The Royal Australasian College of Physicians.

ADMISSIONS TO FELLOWSHIP.

AT a meeting of the general body of Fellows of The Royal Australasian College of Physicians, held in Brisbane on May 29, 1957, the following were elected and admitted to Fellowship of the College: *Under Article 44*: Professor R. R. H. Lovell, of Victoria. *Under Article 42*: Dr. J. L. Adams and Dr. J. D. Willis, of New Zealand; Dr. R. C. Angove, Dr. W. M. Irwin and Dr. R. A. A. Pellew, of South Australia; Dr. G. C. de Gruchy and Dr. H. J. Sinn, of Victoria; Dr. G. V. Hall, Dr. A. J. May and Dr. T. E. H. Spark, of New South Wales; Dr. H. W. Johnson, Dr. W. G. Livingstone, Professor J. H. Tyrer, Dr. L. D. Walters and Dr. H. G. Wilson, of Queensland.

ADMISSIONS TO MEMBERSHIP.

THE following candidates, who were successful at an examination held in New Zealand, were admitted to membership of the College on May 28, 1957: Dr. N. H. Brooke, Dr. D. G. Campbell, Dr. D. R. Hay, Dr. I. C. Isdale, Dr. W. B. Jackson, Dr. B. J. Kelly, Dr. G. B. Kiddle, Dr. R. G. Lawrence, Dr. C. M. Luke, Dr. C. A. Macleod, Dr. D. J. K. North, Dr. L. H. Stevens and Dr. R. C. Tait.

The following candidates, who were successful at an examination held in Australia, were admitted to membership of the College on May 28, 1957: Dr. P. D. Breidahl, Dr. B. M. King, Dr. I. H. McKenzie, Dr. M. L. Mashford and Dr. P. J. Nestel, of Victoria; Dr. H. A. Copeman, Dr. N. J. Nicolaides and Dr. W. S. Rowe, of Queensland; Dr. D. J. Deller, Dr. A. H. Gibson, Dr. D. J. Harbison, Dr. E. J. Lines and Dr. A. P. Skyring, of New South Wales. Dr. R. A. Barter, of Victoria, was admitted to membership under the provisions of Article 37.

The College of General Practitioners.

NEW SOUTH WALES FACULTY.

Pfizer Post-Graduate Lecture.

BY courtesy of the Post-Graduate Committee in Medicine in the University of Sydney, the Pfizer Post-Graduate Lecture is to be given by Dr. Daniel G. Morton, Professor of Obstetrics and Gynæcology in the University of California School of Medicine, and Director of the American Board of Obstetrics and Gynæcology. The lecture will be given at the Stawell Hall, The Royal Australasian College of Physicians, 145 Macquarie Street, Sydney, on Wednesday, August 14, 1957, at 8.15 p.m.; the subject is "Office Gynæcology". All medical practitioners are cordially invited to attend.

Notice.

THE CIBA FOUNDATION AWARDS.

A PANEL consisting of Professor C. H. Best (Toronto), Professor E. Braun-Menendez (Buenos-Aires), Professor E. J. Conway (Dublin), Dr. G. W. Corner (New York),

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED JULY 13, 1957.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	5	5(5)	4(3)	1	..	..	..	..	15
Amœbiasis	..	1(1)	..	..	..	..	..	..	1
Ancylostomiasis	4	..	..	..	..	..	..	..	4
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	1	1	..	..	..	..	..	..	2
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	1(1)	..	..	..	..	..	..	1
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	1(1)	14(13)	..	..	..	..	1	..	16
Diphtheria	1	..	1(1)	..	..	..	..	..	2
Dysentery (Bacillary)	..	..	..	..	1(1)	..	..	..	1
Encephalitis	..	2(2)	..	..	1(1)	..	..	..	3
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	1(1)	..	..	..	..	..	..	1
Infective Hepatitis	39(17)	22(11)	3(2)	1	3(3)	..	..	..	68
Lead Poisoning	..	..	..	..	..	..	..	..	..
Leprosy	..	..	..	..	..	..	..	..	..
Leptospirosis	..	..	1	..	..	..	..	..	1
Malaria	..	..	..	..	..	..	1	..	1
Meningococcal Infection	4(2)	1	1	..	..	..	..	..	6
Ophthalmia	..	..	..	..	..	..	..	..	..
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	1(1)	..	..	..	..	..	..	..	1
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	2	..	..	..	..	..	..	..	2
Puerperal Fever	1(1)	1	..	..	..	..	..	..	2
Rubella	..	31(20)	..	30(8)	8(7)	..	..	..	69
Salmonella Infection	..	..	..	..	..	..	..	..	..
Scarlet Fever	11(10)	25(23)	6(3)	11(6)	2(2)	..	..	..	55
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	..	..	1	..	..	..	1
Trachoma	..	..	..	..	..	..	..	..	..
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	37(32)	18(13)	27(17)	12(6)	5(4)	2	1	1	103
Typhoid Fever	..	..	1	..	..	..	..	..	1
Typhus (Flea-, Mite- and Tick-borne)	..	..	2	..	..	..	..	..	2
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

Professor A. Haddow (London), Professor V. R. Khanolkar (Bombay), Professor R. Nicolaysen (Oslo), Dr. A. S. Parkes (London) and Professor F. Verzar (Basle), with Professor F. G. Young (Cambridge) as corresponding member, has considered 62 papers from 22 countries for the Ciba Foundation's awards for 1957 for research relevant to the problems of aging, and the following awards have been made (the names of leading authors only are given):

Hedwig Saxl (Leeds), £350; G. F. Wilgram (Toronto), £350; R. J. Boucek (Miami), £300; B. T. Donovan (London) and J. J. van der Werff ten Bosch (Leiden) (jointly), £300; R. F. Hellon (Oxford), £300; H. G. Isler (Montreal), £300; L. Haranghy (Budapest), £200; Patricia Lindop (London), £200.

The awards are being offered again in 1958, the closing date for entries being January 1, 1958, and further information may be obtained from the Ciba Foundation, London.

Australian Medical Board Proceedings.

NEW SOUTH WALES.

THE following additions and amendments have been made to the Register of Medical Practitioners for New South Wales in accordance with the *Medical Practitioners Act*, 1938-1957:

Registered medical practitioners who have complied with the requirements of Section 17 (3) and are registered under Section 17 (1) (*a*) of the Act: Dowell, Maurice Francis, M.B., B.S., 1951 (Univ. Melbourne).

Registered medical practitioners who have complied with the requirements of Section 17 (3) and are registered under Section 17 (2) of the Act: Kolobov, Antonin Fedorovitch, M.D., 1917 (Univ. Dorpat).

Registered medical practitioners who have complied with the requirements of Section 17 (3) and are registered under Section 17 (2*a*) of the Act: Milder, Emil, M.D., 1929 (Univ. Prague); Newman, Charles Kurt, M.D., 1939 (Univ. Brno).

Registered medical practitioners who have complied with the requirements of Section 17 (3) and are registered under Section 17 (2*a*) of the Act: Haszler, Charles, M.D., 1931 (Univ. Budapest); Petrauskas, Leonas-Eugenijus, M.D., 1943 (Univ. Kaunas); Svirklys, Maksas Mykolas, M.D., 1930 (Univ. Wilno); Tuza, Francis Louis Charles, M.D., 1943 (Univ. Budapest); Szeps, David, M.D., 1939 (Univ. Lausanne).

Nominations and Elections.

THE undermentioned has applied for election as a member of the New South Wales Branch of the British Medical Association:

Berkowicz, Leon, registered in accordance with the provisions of Section 17 (2A) of the *Medical Practitioners Act*, 1938-1957, 6/98 Coogee Bay Road, Coogee, New South Wales.

The undermentioned have been elected as members of the New South Wales Branch of the British Medical Association: Marshall, Anne Veronica, M.B., B.S., 1957 (Univ. Sydney); Paine, John Lansdell, M.B., B.S., 1957 (Univ Sydney); Grady, James, M.B., B.S., 1953 (Univ. Sydney).

The undermentioned has been reelected as a member of the New South Wales Branch of the British Medical Association: Unwin, Philip Edmond Ralph Byrom, M.R.C.S. (England), L.R.C.P. (London), 1938.

The undermentioned have been elected as members of the Western Australian Branch of the British Medical Association: Childs, Peter Anthony, M.B., B.S., 1953 (Univ. Adelaide); Kakulas, Byron, M.B., B.S., 1956 (Univ. Adelaide); Lobascher, David John, M.B., B.S., 1955 (Univ. Adelaide).

Medical Appointments.

Dr. W. V. Rowe has been appointed an honorary clinical assistant to the surgical section at the Royal Adelaide Hospital.

Dr. P. R. Hodge has been appointed honorary registrar to the professorial unit at the Royal Adelaide Hospital.

Pursuant to the provisions of Section 10 of the *Mental Defectives (Convicted Persons) Act*, 1939, of New South Wales, Dr. D. C. Maddison has been appointed a member of the Visiting Committee constituted under the Act.

Dr. F. H. Garlick has been authorized to sign permissions and certificates for cremation, and to grant permission to cremate any human body after death for the State of Queensland.

Dr. M. Y. Sheppard has been appointed Honorary Clinical Assistant to the Surgical Section of the Royal Adelaide Hospital.

Deaths.

THE following deaths have been announced:

ALTMANN.—Albert Adolph Altmann, on July 8, 1957, at Frankston, Victoria.

WALSH.—Patrick Redmond Walsh, on July 19, 1957, at Brisbane.

Diary for the Month.

AUG. 6.—New South Wales Branch, B.M.A.: Organization and Science Committee.
AUG. 7.—Victorian Branch, B.M.A.: Branch Meeting.
AUG. 7.—Western Australian Branch, B.M.A.: Branch Council.
AUG. 9.—Tasmanian Branch, B.M.A.: Branch Council.
AUG. 13.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
AUG. 19.—Victorian Branch, B.M.A.: Finance Subcommittee.
AUG. 20.—New South Wales Branch, B.M.A.: Medical Politics Committee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

Queensland Branch (Honorary Secretary, 88 L'Estrange Terrace, Kelvin Grove, Brisbane, W.1): All applicants for Queensland State Government Insurance Office positions are advised to communicate with the Honorary Secretary

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2-3.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

SUBSCRIPTION RATES.—Medical students and others not receiving THE MEDICAL JOURNAL OF AUSTRALIA in virtue of membership of the Branches of the British Medical Association in the Commonwealth can become subscribers to the journal by applying to the Manager or through the usual agents and booksellers. Subscriptions can commence at the beginning of any quarter and are renewable on December 31. The rate is £5 *per annum* within Australia and the British Commonwealth of Nations, and £6 *per annum* within America and foreign countries, payable in advance.